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The publication on page 1 of Supplement VII of the Acta Morphologica is the work of two authors. Owing to a technical error, the name of one of the authors has been omitted. Please fix the annexed correct wording in the appropriate place.

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PLENARY SESSION

Recent research concerning transplantation and the fate of plastics in the organism

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The actual problems of transplantation, with special reference to the role of function

The present review is intended to emphasize the role of function, the introduction of which into the modern transplantation literature supported by experimental evidence, should be considered to be a novelty.

Although the importance of function in the fate of grafts had been stressed in numerous earlier reports and publications (1885—1912), this feature has been left unconsidered in the literature of the past four decades. Throughout the world there is a tendency to ascribe the failure of homotransplantations mainly to tissue incompatibility and the efforts are concentrated on the influencing of that factor, hoping thereby to approximate the ultimate solution of the problem. In the following, we shall discuss the effect of function on transplanted tissues, the role of the former in the "take" and viability of grafts in the light of experimental evidence.

There is abundant evidence, both favourable and infavourable, in the literature concerning periosteal grafts. In 1951, *Krompecher* observed that the periosteum of the adult individual may have qualitatively two kinds of activity, viz. 1. osteoblastic bone-building activity, as occurs in activity hypertrophy, and 2. osteoclastic activity by osteoclast-giant cells (differentiating also in the cambium layer of the periosteum, as occurs in disuse atrophy. The bone-producing periosteum adheres firmly to the bone, while that active in resorption can easily be raised from the bone. On the basis of experiments carried out in 1954, *Krompecher*, *Dobi* and *Cseppentő* have pointed out that it is only the bone-forming periosteum that is suitable for grafting for the purpose of bone production. Periosteal tissue grafts should be taken exclusively from bone in the state

of activity hypertrophy. If, by ignoring this principle, the periosteal graft is taken from operated, plaster-fixed bone, or from bone in the state of disuse atrophy due to pseudoarthrosis, the periosteum with bone-resorbing activity will continue to break down bone after it has been transplanted. It has also been shown in the above experiments that by controlling functional relations it becomes possible to determine the quality of periosteal activity.

For example, the bone or limb chosen to serve as the source of the graft may be activated prior to operation. The postoperative functional activation of the acceptor area is just as important, because the fate of the graft, as far as its qualitative and quantitative functions are concerned, will be more and more under the influence of the recipient system.

Before dealing with bone grafts, it has to be pointed out that bone is not a bradytroph tissue. On the contrary, it has intensive metabolic activities. In the field of bone transplantation distinction should be made between auto-, homo- and heterografts.

1. There is universal agreement in that that best results can be obtained by use of autografts. These, however, necessitate another operation on the injured or diseased patient. In spite of the good results, some authors still doubt that the autografts would be superior to homografts in every case.

2. The homograft, if it "takes", does not differ from the autograft in the histologic pattern of unification with the recipient tissue. A study of the pertaining data in literature will reveal that the resorption of homogenous bone grafts is not uncommon, especially when they have been transplanted into soft tissue. Preservation of bone by maceration, freezing, boiling, treatment with merthiolate, deep-freezing, lyophilisation *etc.*, has been given increasing attention in the field of homotransplantation. It is important that the above procedures do not destroy the osteogenetic substance described by *Vereby*, and later by *Levander*. The latter author has shown that the osteogenetic substance is soluble in alcohol, while *Roth* reported that it is destroyed on boiling. Alcoholic preservation for one or two days does not result in the extraction of the total amount of this substance from bone tissue. Excessive cooling (freezing) will destroy the osteogenetic factor of bone. A figure presented by *Roth* shows that the fresh autograft implanted in soft tissue, although it is rapidly resorbed, continues to have a marked osteogenetic activity. The same applies to the fresh homograft. The homograft cooled to $-4°$ C will be resorbed less rapidly, but its osteogenetic activity is less marked and develops only after some delay. The graft stored at $-35°$ C remains almost completely unresorbed, but has very slight osteogenetic activity. The homograft preserved by boiling is not resorbed, but has no osteogenetic activity whatever. This kind of graft is demarcated by connective tissue.

Syngenesioplasty, which shows less tissue incompatibility, emerges from among the homografts.

3. The transplantation of heterografts results in marked tissue incompatibility. This can be lessened by preservative treatment of the graft which, however, will lose its osteogenetic activity during preservation.

A survey of the date and views concerning auto-, homo- and heterotransplantation will reveal that much uncertainty and often contradictions can be found in this field, due to the fact that more than once even the autograft has been absorbed. This has created some confusion, especially in comparative experimental work. The commonest method of studying tissue incompatibility is to transfer the bone grafts by the same technique into soft tissue, in order to determine how the organism reacts to them. This procedure appeared suitable for the purpose of comparison, yet the results were remarkably contradictory. The cause of this is now known. The experimenters did not take into account the function and the shape of bone.

In the experiments carried out by *Krompecher* and *Pap* involving the transplantations of joint cartilage with bone cortex in more than 40 cases it has been found that early exercise i. e. function, is of great importance in the success of transplantation. The recognition of this fact is correlated with the finding that under the influence of adequate function some kind of tissue can be induced to develop at the new site.

Thus, if at some site we ensure a function that will promote the development of a certain type of tissue *(e. g.* bone) from the reserve cells there present, the chances of successful transplantation will be enhanced, because the environment is ready not only to accept, but also to produce such tissue. Thus, the conditions for acceptance, union and regeneration are better ensured.

Let us examine the course of union of a spongious bone graft, allowing it adequate function. It is pointed out in this connection that the process of union is similar in auto- and homoiotransplantations.

As determined at different intervals after transplantation (from 8 days to 2 years), the joint cartilage graft, which has been kept functionally active, and only when it has been kept thus active, presents the histological pattern of an intact, live cartilage, even after homoiotransplantation *(Fig. 1.)*.

As the first step in the union of the spongious bone graft, the bone marrow that has remained in the tissue spaces of the graft will perish. However, this will be followed soon by a gradual growth of granulation tissue into these spaces. After granulation tissue has grown in and invaded the transplanted spongiosa trabecules, capillary vascular buds proliferate in the spaces of the spongiosa graft and within a relatively short period of time (30 days) most of the graft is filled by vascularised granulation tissue.

The proliferation of granulation tissue and vessels is immediately followed by a process essential for organisation of the graft, by the process of appositional bone formation, which starts in the parts of bone adjacent to the wound bed of the recipient and extends thence toward the surface of the cartilage *(Fig. 2.)*.

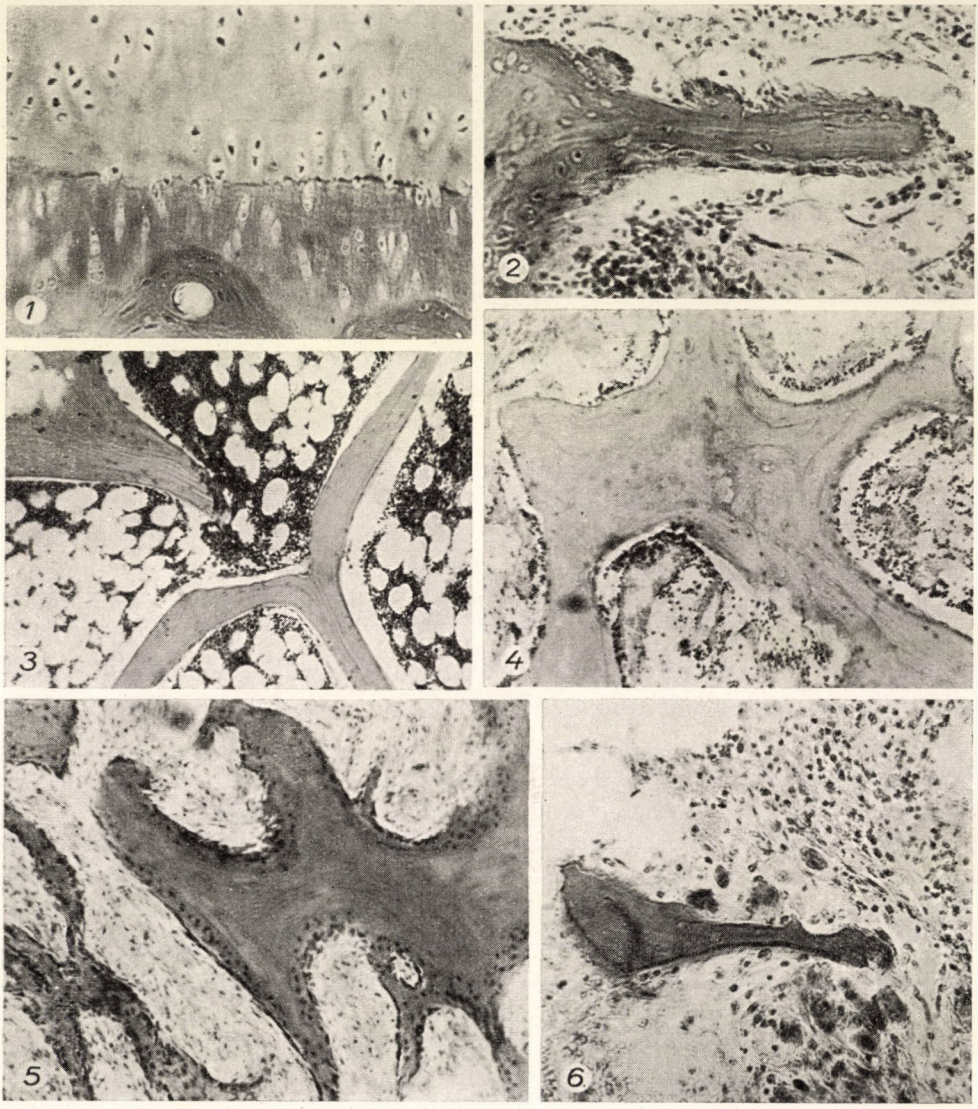

Fig. 1. 2 years 42 days old homotransplant of joint cartilage with cortical bone, exposed to functional stress. The pattern corresponds to that of normal joint cartilage. Haematoxylin-eosin. Magnification, × 230. — *Fig. 2.* Bone formation by apposition on spongiosa trabecules, 22 days following homotransplantation. Haematoxylin-eosin; × 240. — *Fig. 3.* Trabecules of an average diameter of 80 micra in the recipient bone. Haematoxylin-eosin; × 110. — *Fig. 4.* Thick layers of new bone have deposited on the originally 80-micron thick trabecules of the bone homograft. The average diameter of the thickened trabecules is 170 microns. 170 days after transplantation. Haematoxylin-eosin; × 110. — *Fig. 5.* The sheath of new, live bone on the died off bone graft acts as a prosthesis and can be distinguished from the former on the basis of the absence of nuclear staining. 53 days after homotransplantation. Haematoxylin-eosin; × 110. — *Fig. 6.* Breakdown of bone in spongiosa trabecules not involved in function. 22 days after homotransplantation. Haematoxylin-eosin; × 240

As a result the spongiosa trabecules increase in diameter, from the average 80 microns *(Fig. 3.)* to 170 microns *(Fig. 4.)*.

However, histological examination of the spongiosa trabecules of the graft reveals that the osseous tissue in the axial part of the thickened trabecules corresponding to the original graft is necrosed, and the lacunae are empty. On this necrosed bone is built up the new, live bone, which is easily recognized from the presence of bone cells showing good nuclear staining and on the surface of which an osteoblast coat, continuous at many sites can be seen *(Fig. 5.)*. The mentioned increase in the diameter of the spongiosa trabecules in the graft is the result of this appositional bone formation. This phenomenon should be attributed great significance. The structure of the bone graft could meet the demands of the new environment only partially or not at all, therefore, as a result of the new functional requirements, single trabecules became thickened corresponding to the direction and measure of exposure, while others, superfluous from the point of view of functional exposure, were resorbed. Thus, in the graft bone resorption can be seen alongside bone formation *(Fig. 6.)*. As a result of the harmonious coöperation between osteoblasts and osteoclasts, a new trabecular network develops, which can meet the functional demands of the new environment. The recipient system, under the influence of functional exposure, accepts the graft as a prosthesis, builds new live bone tissue on it, breaking down the superfluous trabecules at the same time.

The role of function in the organisation of the graft is clearly illustrated by the control experiments, in which spongiosa grafts were transplanted into areas not exposed to functional stress, for example into gluteal muscle. In such areas within a short time (45 days) various signs of resorption appeared in both osseous tissue and the cartilage covering it.

It has been mentioned that the trabecules of the original graft perish and new, live osseous tissue is formed on them. The question arises whether the osteoblasts, which have been transferred into the recipient system in the graft, multiply and take part in the formation of these new osseous lamellae in the recipient organism, or whether the cells of the granulation tissue in the host differentiate into osteoblasts? In this respect distinction should be made between autotransplants and homotransplants. While in the case of autografts the transferred surviving osteoblasts may play a role in the formation of new bone, in the homo-grafts (as uniformly indicated by each of the preparations) the cells of the proliferating granulation tissue differentiate to osteoblasts and these should be held responsible for bone formation.

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A review of the literature on the results of tissue and organ transplantations shows that only the autotransplantations have been fully successful. The homo-

grafts survive, apart from exceptionally fortunate cases, for some time only (as it has been seen, under functionally adequate conditions this may be extended to several years), after which they are broken down by the organism and serve as substitutes only as long as the organism does not provide for replacement (the functional substitution of *Oppel*). The failure of homoiotransplantation initiated extensive investigations in which efforts have been made to elucidate the causes of resorption and, in the recognition of these causes, to prevent the resorption of the homografts. According to the most widely accepted and corroborated theory, the failure of homotransplantations is due mainly to tissue incompatibility in consequence of differences in the individual protein structures. These investigations have revealed that the failure of transplantations is based on an immunological reaction, with the graft as the antigen, to which antibodies are formed in the recipient organism.

After the role of tissue incompatibility and immunological relations had been recognised numerous attempts were made to influence the immuno-biological relations of the donor and the recipient in order to increase the chances of successful transplantation. The survival time of grafts was in some cases prolonged by using embryonic tissue grafts, by the use of temporary parabiosis, by acting upon the reticuloendothelial system (blocking, x-ray irradiation ect.), by administration of antihistamine drugs, by prolonged sleep, cortisone treatment, but ultimately the desired end could not be attained. Likewise, uncertain results were achieved by inducing changes in the donor tissue (by freezing, heating, preservation etc.).

From this brief survey of the present state of the problems of transplantations one can draw the conclusion that significant results have undoubtedly been achieved. Yet, the number of unsolved points is still great. It is no exaggeration that tissue incompatibility constitutes the problem which gives most concern in this field throughout the world and the efforts of many research workers are concentrated on its solution.

We have endevoured in this review to call attention to the role of function alongside that of tissue incompatibility. Before returning to the problem of function, it should be given due consideration whether it is justified to raise and place into the axis of a review a factor, which in the past 40 years has been left unconsidered in the literature on the very actual and extensively discussed problem of transplantation.

There are few data in the literature concerning the importance of the role of function in transplantation and in the organisation of grafts. *Leriche* has brought up the problems in a work published this year. But how did he do it? In studying the mechanism of vascular neogenesis, Leriche has failed to find answer to a series of questions and while putting forward theories he raised with a question mark the significance of function, within the group also including tropism and finality. The reviews published during recent years contain no

evidence indicating that function would play a role of any importance in the fate of grafts. *Roth*, in his book published in 1952, went as far as to state that one of the conditions ensuring the success of heterogenous bone grafts is that they should be placed into an environment not exposed to mechanical stress. In 1953, *Lopashov* and *Bikman* discussed the actual problems of transplantation and although they have taken into account the question of function they did not publish concrete data, nor did they describe investigations in this direction.

Let us sum up what data we can contribute to the role of function in transplantation.

1. In a work carried out by one of us in collaboration with *Dobi* and *Cseppentő* it has been found that in the case of periosteal autotransplants the functional activation of the latter is of significance and activation should be begun already in the donor. Moreover, the subsequent behaviour, qualitative and quantitative, of the autograft, is profoundly influenced also by the function of the recipient organism. The latter will increase in importance as time passes.

2. In the series of autogenous and homogeneous transplantations of articular cartilage together with the cortical layer, carried out by one of us in collaboration with *K. Pap*, it has been shown that the role of function was decisive, indicating that function would decide the fate of both auto- and homografts. In a series of 3 experiments it was invariably the autotransplant not exposed to functional stress that perished. At the same time, the homograft exposed to functional stress became organized in all 14 out of a total of 14 well-evaluable cases. To this may be added that one of the two swine bone grafts transplanted into dogs (1) showed signs of partial organisation.

3. According to the investigations of *Altmann*, dead bone, if it is inserted into a static system and is given a supportive role, behaves like live bone. It will not be broken down by osteoclasts, on the contrary, new, live layers of bone will be formed on both of its surfaces.

4. In the tubular bone transplantation experiments of *Vereby*, as well as of *Dobi* and *Cseppentő*, a peculiar functional situation has arisen. As a result of the tubular shape of the graft a functional system developed, with the perforation of the tube and with the development of new trabecules in the marrow cavity. We are of the opinion that the development of this functional system, which is biological, biochemical in nature, will ensure for several months the survival of the graft, or at least the development of a new structure in it. This example illustrates clearly the important role played in bone formation by the osteogenetic substance released when bone is being broken down.

5. Dealing with tendon-grafts, *Lange* writes in his book that pieces of tendon have been successfully replaced by a strip of cutis *(Rehn)* and by the saphena magna vein *(Ritter)*. In the light of modern knowledge concerning function, the process can be properly evaluated.

6. The role of function in the case of vascular grafts can be interpreted in a similar way. According to *Guthrie*, a vein transplanted from one animal into another survives only if the graft had been placed into a blood vessel, i. e. it was connected into the circulation. Vascular graft transplanted into muscle or other tissue perished.

7. The role of function becomes manifest also in endocrine gland transplantations. For example, the thyreoid transplantation is more successful, when carried out in a previously thyroidectomized animal.

It is believed that these concrete cases, although small in number, call attention to the fact that in addition to tissue imcompatibility function has also to be credited with an important role in the field of transplantations.

It is a difficult task to compare the role of function with that of other factors, such as tissue incompatibility. It can be assumed that such a comparison would yield different rations as soon as different organs or tissues are examined in their quality of hetero-, homo- or autografts. At present, endeavouring to emphasize the role of function in transplantation, it may be relevant to make a comparative analysis in a given case, notably in that of bone transplantation. It is known from literature that views concerning the fate of auto-, homo- and heterotransplants greatly diverge. However, when evaluating their results, the authors have ignored the role of function. In the light of the experimental evidence obtained by us it can now be stated that function plays a decisive role in the fate of bone grafts. We have shown that in one and the same animal autotransplant left without function will be resorbed, while, disregarding tissue incompatibility, the functionally active homograft will be organised and tolerated merely as a prosthesis, for months or even for years.

Thus, in these bone transplantation experiments function proved to be a factor more important than tissue incompatibility. It seems that function plays a role also in endocrine gland transplantations. In the knowledge of its role in the qualitative development and quantitative growth of tissues, it seems justified to study the role of function also in the transplantation of other tissues.

In the foregoing we have discussed the problem of function *versus* tissue incompatibility. To outline the correlation between the two, the following points are emphasized on grounds of experience obtained in cases of spongiosa transplantation.

1. If the spongious bone transplanted is not made to function, to bear adequate stress, it is broken down by granulation tissue. The protein-like breakdown products act as antigens and the antibodies produced to them by the recipient organism create even more unfavourable conditions for the graft, which will be broken down at an accelerated rate.

2. In contrast with this, when the transplanted spongiosa graft is exposed to functional stress, single, more exposed trabecules in it will respond to the stress with an increased tendency to activity hypertrophy. The undifferentiated

cells of the granulation tissue invading the graft along the trabecules will differentiate into osteoblasts and appositional bone formation will begin immediately on the surface of the trabecules, forming a sheath on the latter. The thickening of the organised trabecules is clearly visible.

Thus, the exposure of the transplant to adequate functional stress acts against tissue incompatibility in two ways : 1. The functionally active tissue is broken down at a slow rate, and 2. the new bone sheathing the graft leaves behind less surface exposed to breakdown and thus breakdown becomes slower. In time, the organised trabecules are broken down in the course of reorganisation, but this process hardly exceeds the extent of physiological reorganisation and gives rise to no allergic reaction which would accelerate resorption of the graft.

The significance of function and its sequelae should be examined in different types of tissue. It is obvious that patterns similar to the sheathing of bone trabecules will hardly occur. However, the inhibitory action of functional stress on resorption or breakdown may be manifest in other tissues and organs, too, and it may even result in a certain increase in the number of transplanted cells of the autograft, as it has occurred in the cases of periosteal grafts described above.

As shown by its title, this review has been intended to place the role of function in a proper light. Relying first of all on our investigations into bone transplantation, it has been shown that function also plays a role in transplantation and, especially in the case of spongiosa grafts, the role of function was more significant than that of tissue incompatibility. It has been demonstrated experimentally that without function even the autotransplant will be resorbed, while if adequate function is ensured, not only the autotransplant, but, disregarding tissue incompatibility, also the homotransplant may be organised for months or years, although merely as a prosthesis. It is the task of the immediate future to examine the role of function in transplantations involving different organs and tissues and to determine in what measure function may counterbalance the inhibitory action of tissue incompatibility. This task can be summed up in one sentence : Attempts should be made to counteract the deleterious action of tissue incompatibility and, by ensuring adequate function, to enhance the success of transplantation.

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The fate of plastics in the live organism

Plastics and resins neutral to tissues are being more and more extensively used in various branches of medicine and thus it is time to review briefly the possibilities of their use and to follow up the fate of such materials after implantation into the organism. There is obviously no place within a short review for discussing all possibilities plastic materials offer to modern medicine and thus their use in bone and joint surgery, as well as in stomatology will be dealt with in brief only, this being a rather well-known topic. In the latter connection only a few statements will be made, which seem essential for a better characterisation of single plastics. The plastics used in our special branch will not be dealt with one by one and in more detail, since they have a variety of properties in common.

Plastics are understood to mean compounds of well-defined chemical structure, produced mainly by synthesis, they now number several hundreds. There are, however, also plastics prepared from animal or plant materials. Among the latter have been listed by *Thinius* (1952) the different resins, gelatine, cellulose, and we may add to the list fibrin. Other alloplastic substances, such as for example the metals and alloys are not plastics, altough they are neutral to the tissues, yet, as far as their origin is concerned, the are distant from plastics.

I. Most of the synthetic substances used in medical practice are polymerisates, thus they consist of long chains of molecules and it is the latter that determine the properties of the various materials.

1. The properties of the polymerised methyl methacrylate, artificial resin or plexiglass, will be dealt with in more detail, this being the most widely known plastic material and the one most widely used in medical practice. In recent years, numerous reports have been published on its use in surgery, though it had been used for long in stomatology and a variety of preparations had been made available to meet dental requirements. Since its properties are in many respects excellent, and in view of the versatility of its use, it seems justified to present a description of its physico-chemical, mechanical and biological properties and of the results of recent investigations concerning its application.

The patent describing the synthesis of polymethylmethacrylate was published in 1928. The basic ingredients of polymethylmethacrylate are acetone and HCN. The monomer is a water-clear, inflammable fluid, which can be polymerised in the presence of specific catalysts by exposure to heat, light and pressure. The polymer consists of long molecular chains (several thousand mole-

cules) and, unlike the monomer, wich has a highly toxic local action, it is neutral to tissues. Especially when produced for industrial use (i. e. when the toxicity of the monomer plays no role), polymerisation may be imperfect, and the material contains a certain amount of monomer and also short-chain polymers which in time become depolymerised under the influence of various effects.

The physico-chemical properties of artificial resin make it an excellent material for medical use. Though these properties may vary from preparation to preparation, the average values may be given as follows : specific gravity 1,16 to 1,2 ; light refraction index, 1,49 to 1,51 (this being significant in view of the fact that attempts have been made to use it to replace the lens after cataract operation) ; melting point, around 120° C (but there are plexiglass preparations which become plastic at temperatures as low as 70 to 90° C). Where an endoprosthesis made of plexiglass is exposed to excessive stress it is important that it keeps its shape and should not break. The blockpolymer used for such a purpose is translucent like glass, poreless, colourless, odorless, tasteless, slightly elastic and permits the passage of most ultraviolet rays. It has a great tensile and bending strength. It can be worked upon excellently, it can be born, sawn, turn on a lathe, and ground. It is well sterilisable. The endoprostheses made of artificial resin can be combined with metals, because electrolytic phenomena do not arise, it being an excellent insulator of electricity and heat.

On the other hand, some of its properties may make its use risky in the presence of excessive mechanical stress. The first of these properties is material fatigue, which has been observed to occur especially in arthroplasty of the hip joint. After it had been in place for several years, corrosion may appear on the surface of the prosthesis, resulting in a loss of strength and, ultimately, in breaking. This circumstance has less significance when exposure is less intensive, as for example in case of vascular prostheses *(Bornemisza)* to which I shall return later.

In general, plexiglass is resistant to acid and alkali, and is soluble in benzene, ketons, ether and aromatic hydrocarbons.

From our point of view, the biological properties of the material are the most important. It is desirable that it contains the lowest possible percentage of the monomer, or of the easily depolymerised short-chain polymers. The results of imperfect polymerisation were observed most often by dentists treating caries, when the material injured the pulp. The monomer in touch with the oral mucosa causes ulceration.

The first histological studies of artificial resin implants have been made by *Mac-Kensis*, *Spealman* and *Beck* (1945). *Starck*, *Menegaux* and others have examined the behaviour of the material in tissue cultures and found that it did not diminish cell activity, nor did it cause cytotoxic reaction. According to data n literature, *Zander* and *Kleinschmidt* were the first to use it for the replaement of cranial bones (1941). Later, its use has become more and more wide-

spread especially in reparative surgery (surgery on the organs of motion, replacement of the back of the nose, ear and mandible *etc.*). In 1943, *Harmon* recommanded its application in joint surgery, preceding thereby the *Judet* brothers. In 1954 *Hufnagel* and his associates made of artificial resin a ball valve, which has been used for the repair of the insufficient aortic valve; apart from a considerable number of animals, the procedure was successful by 17 patients. *Weiss* (1954) placed the ball into the heart to correct valvular insufficiency and obtained favorable results.

I have carried out successful experiments involving the replacement of blood vessels by plexiglass tubes. This procedure has been applied in foreign contries, too, and recently *Hufnagel* has reported on good results. The use of the material for this purpose is based on the fact that the tube made of it is sufficiently resistant and is not absorbed, it can easily be sterilised and on its smooth surface clotting time is prolonged. Attempts have been made to use plexiglass for the substitution of oesophagus, trache, choledochus and urether. In addition to its application in dentistry, plexiglass prosthesis are in use in ophtalmology as artificial eyes and as small balls for filling thoracic cavities. The material has lent itself well for the preparation of anatomical and histological models.

In the course of my experiments to replace vessels I have found that plexiglass preparation made in this country by the Research Institute for Plastic Materials is suitable for surgical purposes. The tubes used for replacing blood vessels are very soon surrounded by a loose network of very fine collagen fibres, the interspaces of which are first filled with fibroblasts, and later, when the collagen fibres increase in number and are arranged to form thick bundles, a capillary network develops in the capsule, which may reach a thickness of 1 mm. This plexiglass preparation has been used by us (in cooperation with *K. Pap*) also in bone surgery and the results were satisfactory in every respect. X-rays revealed an increase in density around the plexiglass in place, a sign that the material caused a contact proliferative reaction. A plexiglass cylinder was implanted in bone ; between it and the bone canal the connective tissue layer soon developed, showing the characteristics described above. In recent experiments we have made use of the turnings of the plexiglass turned on the lathe. They being resistant to most chemicals, the turnings could be mixed with antibiotics and chemotherapeutics and so used in infected areas, too. Turnings enclosed in nylon mesh have been used with succes as a plombage in experimental thoracic surgery. In time the interspaces between the turnings are filled with connective tissue, which shows abundant vascularisation.

2. Nylon (polyamide, Igamide *A*) was invented also in 1928. It is nearly identical with perlon (Igamide *B*), related compounds being supramide, caprone, silon, pehafil. All these are synthetic materials, with a melting point around 110 to 215° C. Nylon threads have been applied in surgery for 5 years now and,

being extremely strong, elastic, hardly or not absorbable, it has proved to be an excellent material for suturing. In elasticity and tensile strength, nylon threads are superior to any textile thread. According to a recent report by *Schmitt* (1955), nets made of perlon were successfully used for repair of the abdominal wall and inguinal hernia, in nephropexy and plastics of the breast. Melting and cooling the perlon, endoprotheses suitable for nasal, ocular, facial, bone, skull and joint correction have been made of it. Animal experiments and histological studies have shown that it does not cause inflammation and induces, like the afore-mentioned agents, connective tissue proliferation. The strength of nylon, too, is dependent on the length of the polymeric chain. Nylon is colourless, odorless, tasteless and excellently stainable. It is insoluble in most chemicals. I have sterilised nylon by boiling it in Rifen solution, with excellent results.

3. The vinyl derivatives, too, have been successfully employed by different authors. In this country *Hedri* and al. has carried out osteosynthesis experiments with polyvinylchloride (PVC), a material becoming mouldable at a low temperature. A plastic material of a similar nature designated EGMASS 12 has been described by *Gruzdkova* in the Soviet Union. It was used in 55 cases of facial and mandibular surgery for the correction of defects, with good results. *Voorhees*, *Jaretzky* and *Blakemore*, and others have obtained certain results in vascular repair with vinyon "N" mesh. In this connection I make mention of polyvinylpyrrolidone used as a plasma expander under the name of Periston, Plasmosan *etc.* It is soluble in water, has a molecular weight of 40 000 to 50 000 and good osmotic qualities. It is excreted in the urine in about 3 days, but part of it is stored in the cells of the reticuloendothelial apparatus, in histiocytes and renal epithelial cells for longer periods of time, as it has been demonstrated by *Jancsó et al.* (1954).

4. Polyethylene, known by the names of polythene, parovax, lupolen H. *etc.*, consists of chains of about 1000 carbon atoms, has a molecular weight of from 18 000 to 26 000 and is insoluble in most solvents. In medical practice it has been used for replacement of dura and cranial bone. Attempts have been made at using in experiments a sack made of polyethylene filled with fibreglass for filling out the space remaining after removal of the unilateral lung. For this purpose, sponges of polyethylene are now available. In the repair of abdominal wall hernia, in vascular surgery, as well as in transfusion technique it has become more and more extensively applied and various catheters have also been made of it.

II. From among the materials of animal or vegetable origin, attention has in recent times been focussed upon fibrin, cellulose and gelatine.

1. In this country, fibrin has been employed by *Gerendás*, *Zinner* and others for creating joints and in experimental vascular surgery. *Salem* lined fibrin tubes with vein and used them for correcting vascular defects. Fibrin has the advantage over the afore-mentioned plastic materials that it is absorbed

by the organism and that the time of absorption can to a certain degree be regulated at production.

2. It is generally known that cellulose and its derivatives are extensively used in industry. Recently, they have been gaining increased acceptance for medical purposes. *Faine* introduced cellulose sponges to replace the tampons used at operations. Similar experiments are in progress at our Institute, with the viscosa sponge produced in this country. Here should be mentioned collodion, the ether-alcohol solution of cellulose nitrate. It has been in use for long for the dressing of surgical wounds and the investigations by *Huzella et al.* (1928) revealed several valuable properties of this material. Collodion tubes were inserted into blood vessels and it was found that 14 days after insertion the internal surface of the tube was covered by endothelium similar to the lining the acceptor vessel. This epithelial coat was formed by the monocytes of circulating blood. Initially, cells with large, round nuclei adhere to the wall of the tube. These subsequently and finally adhere firmly and smoothly to the wall of the tube. In this way had been corroborated the possibility of haematogenic endothelium formation. The findings were subsequently confirmed in the artificial resin experiments of *Weiss*. In my vascular repair experiments, tubes of plexiglass (artificial resin) were covered by collodion and such tubes were used for repairing the defect in the abdominal aorta of the dog. The results were superior to those obtained with plexiglass tubes alone, because on collodion clotting time is also prolonged and thus permanent passage through the tubes could be ensured.

In general, the above materials give rise to only a minimum if tissue reaction, which shows no specific characteristics. As alloplastic materials they were well tolerated altough late results are not yet available in sufficient number.

Little is known of the absorption of plastic materials. To our knowledge plexiglass is not absorbed and perlon is absorbed at a very slow rate, in years. The investigations carried out so far did not reassuringly answer the question whether plastics may not cause malignant degeneration. According to *Karitzky* (1954), this possibility must be taken into account. In clinical and histological studies made with nylon and perlon *Ahsett* and *Druckrey* (1954) could not corroborate this view. It is very difficult to follow up these problems in the common species of laboratory animal, these having a short life span. Thus, one must in this respect rely upon clinical observations and histological studies.

In this brief survey obviously no attempt could be made at completeness and the numerous questions that emerge in connection with plastic materials will, after they have been discussed and answered, effect an ultimate elucidation of these greatly important problems.

CO-RELATOR:

N. Zinner

(State Institute of Rheumatology and Balneology, Budapest)

Significance of artificial substances in orthopaedic surgery

Chemistry has produced artificial substances which owing to their physical and chemical properties are tissue friend i. e. the organism does not consider them foreign bodies to be expelled, but accomodates them as a host for unlimited time. On the other hand, the artificial substance remains in place as an unchanged chemical compound and secures the stability of form and function. In the following, only those artificial substances will be discussed, which the author has gained experience with. 1. Polyamides, first of all nylon. Their structure resembles that of native proteins. 2. Polyvinylchlorides (PVC) made up of 1000 to 2500 chain molecule units. The polymer occurs as a hard product or in a softened form. Some compounds used in softening are poisonous, for instance ortho-tricresyl-phosphate. 3. Polymethyl acrylate, a polymer consisting of 2500 basic molecules. This substance is especially suitable for endoprostheses. 4. So-called natural plastic materials derived from blood, such as fibrin, and muscle. Unlike the former which remain at the place of implantation and secure stable shape and function, these substances are absorbed after their presence had helped to develop the conditions securing function by natural ways.

1. Polyamides were used as nylon plates in arthroplastic operations of the knee joint in 10 cases, of the elbow in 4 cases. No general reaction was observed. Serous accumulations which were repeatedly punctured occurred at the knee and the elbow in 1 case each. The operation invariably resulted in good mobility and stability. The fate of the plate covering one of the joint ends is unknown, since biopsy was not performed and none of our cases was operated again or seen at necropsy. The clinical results are, as judged from a 6-year follow-up, satisfactory.

2. PVC was used in conservative orthopaedics, for fastening splints. *Stefaics* has made of it excellent artificial limbs. The material is well suited also for arch-supports, it being solid at room temperature but pliable at a somewhat higher degree. Our chemist associates have pointed out its three undesired qualities: 1. The occasionally poisoning effect of the softening materials, 2. the possibility of splitting off of hydrochloric acid, owing to the presence in the bone of chlorine atoms, 3. its "cold flow" i. e. the property that its form may change also at a low temperature. The application of this substance is nonetheless desirable, since steel splints in leather capsules are still extensively made.

3. Polymethyl acrylate has been used in replacing bones since 1947. In this country, *K. Pap* was the first to use it a few years later. New bone is formed in 2 per cent of the patients only, much less frequently than after the application

of vitallium. Therefore, motions are less limited than with the latter substance. Complications after arthroplasty with acrylate are rare ; the operation is better tolerated than other operations of this kind. In animal experiments, tibia defects were replaced by acrylate. (A model has been presented.) Recently, it has been tried to perform extraarticular arthrodesis with acrylate plates made radio-opaque by implantation of fine metal threads into the acrylate. These plates have the advantage over bone laths, that organization need not be awaited for several months. The limb can be used immediately after wound healing, complete fixation being seemed by the acrylate prothesis without the application of plaster. In some cases of opponent paralysis, arthrodesis in opposition was performed in this manner, by firmly unifying the 1st and 2nd metacarpal bones. We have also contracted an acrylate case to be applied to amputation stumps ; it can be fastened by simple screwing, without a limb suspension apparatus.

4. In the last year, the fibrin pieces prepared by the author and his associates have been described in a preliminary communication. Now we wish to discuss the clinical results obtained with them. The pieces were used in arthroplasty in 18 cases, and in one instance tendon sheath was replaced by a fibrin tube. In three of our patients suffering from Bechterew's disease, the stiff mandible joint was successfully mobilized with this method by Dr. *Z. Frankl.* In a few cases a serous exudate was formed ; in one of them the fibrin film had to be removed but the mobility of the joint remained unimpaired. Four cases of hip joint arthroplasty were completely cured, without local or general complications or pain. The application of the fibrin tube is recommended in tendon transplantations, in order to prevent the adhesion of the tendon, if it cannot be passed through a tendon sheath, especially in „remote transplantations", such as the replacement of the biceps muscle by the sternomastoid or the major pectoralis muscle with fascia lata lengthening. It seems possible in this way, to transplant these muscles for replacing the flexors of the hand and the fingers, whereby the intractable paralysis of hands can be restituted. In one of our patients the biceps muscle was replaced by the sternomastoid, then shoulder and opponent arthrodesis were carried out with so much success, that now the patient is an excellent sculptor student of the Academy of Applied Arts. He is able to draw, form, and carve. The author thanks dr. Gerendás for the solution of the problem of fibrin caps and other bioplasts. To his knowledge, absorbable arthroplastic pieces were first prepared in this country.

The significance of artificial substances in orthopaedic surgery may be summarized in three points. 1. They represent much facility for both the surgeon and the patient in extensive orthopaedic operations ; they allow the surgeon to perform operations otherwise impossible. 2. One of the most important points in orthopaedic surgery is a correct fixation. For a century this has been done with plaster of Paris. The fixation ensured by artificial substances is far more accurate, and the disagreeable circumstances of plaster dressing fall off. 3. There

is a need for institutes in which a clinical department, a laboratory for animal experiments and a department for technical and chemical research is accomodated and in which specialists can learn from each other and discuss their common problems.

CO-RELATOR:

E. Kubányi

(Hospital No. 1. of the Pest County Council, Budapest)

Transplantation of organs from living persons, dead bodies and from animals (illustrated with motion pictures)

Clinical experience has shown that transplantation of endocrine organs or tissues is needed much more often than it is carried out.

I. In the rare cases in which organs or tissues can be transplanted *from man to man*, it is absolutely essential that

a) both donor and recipient be tested in advance for syphilis by the Wasserman test;

b) that the blood type and

c) the Rh-factor be determined in advance and that both be compatible.

II. Similar rigid criteria should be observed when transplantation is carried out from *animal to man*. In such cases the graft must be

a) fresh and

b) sterile.

Furthermore, it has to be ascertained that

c) neither tuberculosis (12 to 26 per cent) nor brucellosis (20 to 40 per cent) or anthrax infection is transferred.

As it takes considerable time to work up the slaughtered animal and to examine it for the eventual presence of disease, earlier it could not be solved that the organ to be transplanted should be both fresh and certainly not infective. *Rapid freezing* now makes it possible to preserve fresh organs under sterile conditions, in separate dishes provided with adequate registration signs or numbers. Veterinary examination will then decide which of the organs are suitable for use as implants or grafts. This procedure makes it possible to transport in Dewar flasks the organs fast-frozen at the slaughterhouse to the institute, and to implant them within 2 hours, or to store them deep frozen. The introduction of fast freezing has *ultimately simplified the technique* of implantation.

Of the problems of transplantation only those are interesting for the pathologist which offer insight into the correlation between histological studies and clinical results.

The subject matter of the present lecture has been grouped around two problems, in which the clinical observations made on the basis of histological experiments can be illustrated by cinematography. We present, at first,

histological sections obtained in animal experiments concerned with the choice of the site of transplantation. The conclusion drawn from this material is that in transplantation from man to man (be it carried out either with transplants from live or dead bodies) the primary aim is to ensure *survival* of the graft for longer or shorter periods of time.

The graft must be

a) implanted into its appropriate anatomical site, or near to it, and

b) brought into connection with the secretory fibres of the appropriate sympathetic segment.

The *Rossi—Mosinger* schema shows that the pituitary is supplied with secretory fibres from the carotid centre. With due regard to this, we have implanted (motion picture No. 1.) from the mother a parathyroid taken at thyroidectomy into her daughter, who belonged to the same blood group and had the same Rh-factor. The result was excellent and the girl has been free from complaints for two years now.

On the basis of the same principle, from individuals who would have been necropsied compulsorily we removed pituitaries by "sterile section" (motion picture No. 2.) within two hours after death due to traffic accidents, and transplanted them into 7 patients with Simmonds' disease, between the sympathetic fibres of the common carotid.

The second problem concerns the storage of transplants.

The greatest difficulty could be eliminated by the introduction of fast freezing, which has made it possible to bridge over the time lag between the removal of the graft from the donor and its transplantation into the recipient.

In motion picture No. 3. the transplantation of calf pituitary and bovine parathyroid, fast-frozen and stored under deep-freeze, is illustrated. An account is given of the results obtained in the course of 5 years.

CO-RELATOR:

K. Pap

(1st Dept. of Surgery, Medical University, Debrecen)

Transplantation and implantation in surgery and orthopaedics

After a brief survey of the literature the up-todate results and problems of the transplantation of tendons, muscles, bones, und whole limbs, are discussed. Advantages and disadvantages of transplantation and implantation are summarized in connection with a presented case, the first in which in Hungary acrylate was applied in surgical-orthopaedic disease.

It has been observed that acrylate is not quite free of a certain, often late, irritative effect, whereby it may give rise to calcification or ossification. This process is desirable if a bone part is to be replaced, while undesirable in joint formation. Finally, cases of semi-malignant bone tumours bone plombage are reported treated by it.

CO-RELATOR:

K. Tarnai

(Dept. of Stomatology, Medical University, Budapest)

Use of foreign materials in oral-surgery

The substitution of jaw defects with metal appeared to be natural from the outset. However, results were not at all satisfactory. In Hungary the observations of Jenő *Orsós* have called attention to the electric actions of metals set in the organism. The fundamental researches of *Venable*, *Stuck* and *Beach* made it clear that the organism can be regarded as an electrolyte and that the allenthesis has a measurable electrode-potential to which the organism responds with metallosis. For this reason, results can be expected only from electrogenetically inactive metals such as vitallium. Since 1956, at this Department 56 graftings were performed out of which 28 per cent were unsuccessful. The failure could be brought into connection with the casting and elaboration of the metal and with the selection of the cases. A metal allanthesis is an excellent appliance, but can be looked upon only as a palliative and not a final solution, because it does not substitute the organic connection resulting from grafting of the own bone.

DISCUSSION

Behaviour of autogenous skin grafts in chlorophyll milieu

Á. Skutta, Klára Tuza

(Dept. of Dermatology, Medical University Debrecen)

In human experiments, autogenous skin grafts were implanted onto the granulating surface of various skin ulcers at a distance of 3 to 4 cm in order to observe the growth of the epithelium and the interaction of epithelium and granulation tissue. In a chlorophyll milieu more than 95 per cent of the grafts had taken and began to grow. This phenomenon is similar to the well-known growth of mould fungi on agar media. Having attained a size of about 4 cm in diameter, the grafts lose their round shape and approach each other by slender projecting processes, they become fused and the ulcer heals. When the surface of the epithelium is already in excess vigorous movements are started in the granulation tissue and half-nut-sized protrusions and thumb-thick strands arise in a few days spontaneously to vanish in the next few days. These results seem to present convincing contributions to the pathology of autotransplantation (and may be applied in therapy.

Methods for prolonging the viability of dermal homoio-transplantates

Gy. Frank

(Kun utca, Municipal-Hospital, Budapest)

It is a well-known fact that the viability of homoio-transplantates is limited. Yet, derma. homoio-transplantates may have a life-saving effect if large skin defects are to be covered temporarily. It is advantageous to prolong the life of such grafts and for this aim we employ the following methods :

1. Donor and acceptor should belong to the same blood group, also beyond ABO compatibility.
2. Utilization of several donors to ensure that small surface of skin, i. e. little amounts of antigen, should be passed from each.
3. Use of half thickness grafts (0,5—0,6 mm).
4. After the 7th day of transplantation cortisone is administered.
5. Storing the graft at —5° C to —10° C for 1 to 3 days may prolong its life.
6. Homoioplastic and autoplastic grafts are alternately applied to the defect. In this way, the autoplastic epidermis can encroach upon the homoioplastic corium surviving also after the expulsion of its epidermis.
7. Proper preparation of the wound bed.
8. If possible, complete covering of the wound.

Transplantation in septic environment

P. Berényi, K. Pap

(1st Dept. of Surgery, Medical University, Debrecen)

Grafts (skin, bone) disappear by necrosis and absorption. In a suppurating environment there is more probability for necrosis. Experiments have shown that periosteum and bone spongiosa may survive also in a septic environment. Experiments have been carried out to detach a callus which had survived in a septic environment by adaptation to it, and to transplantation it to a broken place or the one of little stability. These grafts survived.

The results of similar transplantations may be explained by assuming that, like other granulations, the callus formed in a septic environment had become resistant to infection, wherefore its growth is not impaired by suppuration.

Fate of arterial transplantates

J. Ormos, L. Sin

(Dept. of Pathological Anatomy and 1st Dept. of Surgery, Medical University, Szeged)

Pieces of dogs' aorta preserved under sterile conditions in :
1. physiological saline containing 10 per cent plasma,
2. 4 per cent formalin,
3. Jores' solution, and
4. 10 per cent mercury oxycyanate,

respectively, further pieces of swine's aorta fixed in 4 per cent formalin, were transplated into the abdominal aorta of dogs. The grafts were histologically examined 4 to 533 days after the transplantation. The connective tissue and smooth muscle elements of the grafts undergo destruction in the first days, except for the elastic fibres. On the inner surface a thick new coat of connective tissue (new intima) forms. After some month the media too is replaced by new fibrous tissue. While this is being formed the intravascular pressure is resisted by the remaining elastic meshwork, until the new intima has developed. The changes in the grafts are independent of the method of preservation, and no marked difference appears between homoio- and heterotransplantates.

Closure in layers of chest wall defects by tissue transplantation

O. Székely, T. Remete, I. Kiss, R. Schneider

(Central Military Hospital and Polyclinic, Budapest)

As a result of a partial loss of ribs and extensive adhesions, large thoracic defects lead to chest deformity. In surgery for the repair of thoracic wall defects the replacement of soft tissue and lost ribs is still an unsolved problem.

In experimental studies aimed at a reconstruction of the osseous structure, free transplantation of ribs obtained from cadavers and preserved by different methods have been carried out. In one group of animals the pleura has been retained and only the costal defects have been repaired, while in the other group a window was cut in the chest and the repair of both pleural and costal defect was carried out in one stage.

Clinical and histological data obtained in 47 operated animals are presented.

The costal graft fixed in formaldehyde behaved as a foreign body in the majority of cases, caused an inflammatory reaction in the environment and was often sequestrized. The rib fixed in formaldehyde proved to be unsuitable for use as a graft, both clinically and histologically. The costal grafts preserved in the dry state at -5, $+5°$C showed the signs of intensive resorption after transplantation and were either totally absorbed or built in with callus formation. The lyophilised costal transplants exhibited a definite tendency rapidly to be built in during the relatively short, five-month observation period. This was confirmed by both clinical and histological observations.

Three phases in the life of heterotransplantates

Gy. Csaba

(Dept. of Histology and Embriology, Medical University, Budapest)

It has been endeavoured to determine the role of assimilation and immunologic factors in the life of heterotransplantates.

Into the anterior eye-chamber of white rats autologous and homologous rat liver, liver of guinea-pigs and salamanders were implanted. The changes occurring in the transplantates were followed *in vivo* by means of a microilluminator, then the eyes were prepared by histologic

methods, finally, the growing capacity and vitality of the tissues were examined by culturing in the serum of the acceptor.

Autologous, homologous and heterologous mammalian liver becomes destroyed within two weeks, except for the biliary ducts of autologous liver from which regeneration is started. Salamander liver displays active growth even after 6 weeks. If, by the end of the 5th week, it is removed and explanted onto a warm-blooded medium in Maximov cultures, the liver and pigment cells likewise exhibit vigorous growth. Unlike this, the other autologous and heterologous liver pieces do not grow after direct explantation and undergo destruction.

The experiments point to three factors influencing the fate of the transplantate in the recipient organism, viz.

1. local traumatism or nutritional disturbance,
2. phase of assimilation-adaptation,
3. phase of production of immune substances.

The experiments seem to show that survival of the transplantate depends on the second phase, inasmuch as after this stage immunbiologic reactions cannot any more have a decisive role, provided the tissues of the transplantate had adapted themselves.

Experimental transplantation of the thyroid gland

I. Dévényi, B. Czenkár

(Dept. of Pathological Anatomy, Medical University, Debrecen)

The conditions have been examined on which the taking and functional survival of homoio-transplantated embryonic and adult thyroid tissue of rats may depend. To this end, Halsted's principle was utilized, according to which the successful transplantation of endocrine organs depends greatly on lack of its hormone in the recipient organism. First, subtotal excision of the thyroids and removal of the parathyroids were done, then the transplantate was placed into a pouch formed in the subcutis of the back. In different series embryonic and adult thyroid, respectively, was used. In these series the transplantate underwent destruction between the 20th and 30th day. Total body irradiation with X-rays, before the transplantation had no effect. In further experiments, 2,5 mg of cortisone were given every other day on six occassions, while other conditions remained unchanged. In this series the transplantate survived in the majority of cases, the embryonic thyroid tissue underwent differentiation and functioned. Because of the shortness of time we could not follow the life of the transplantate beyond the 64th day. Further observations are in course. It seems, however, warranted to consider the results a success. If the thyroid of the recipient animal had not been removed the transplantation was unsuccessful in spite of cortisone therapy.

Animal experiments to influence the state after total or partial parathyroidectomy

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Heterografting with deep-frozen calf parathyroid makes it possible to prevent in the rabbit the simultaneous functional deficiency of all four main parathyroids and thus to protect the organism from tetany. The graft makes its action felt within 24 hours already.

The grafted organ does not become fully integrated into the organism. It succombs successively to a regressive process and accordingly the Ca/P ratio in serum undergoes a change. Degeneration and cell destruction in the graft always begins in the centre of the organ while the peripheral cell-groups bordering on the granulating connective tissue rich in veins remain normal for four weeks, their cell and nuclear structure indicating no essential lesion. 5 to 10 weeks after grafting no more intact glandular epithelial cells can be found. We have observed in a pregnant hare intact tissue in the grafted parathyroid gland 51 days after grafting. In our opinion, the factors responsible for this phenomenon — unusual in a not pregnant animal — are the increased Ca requirement and the hormonal changes connected with gravidity.

Tissue reactions of ovary grafts to administration of gonadal hormone

B. Flerkó, Gy. Illei

(Dept. of Anatomy and Histology, Medical University, Pécs)

The differentiated tissues of ovaries autografted into the spleen of a castrated rat degenerate, with the exception of the primary follicles out of which the characteristic structures of the ovary develop in some weeks provided blood supply and hormonal environment are adequate. This process is not damaged by progesterone treatment (400 μ g/day), because, as also in ovaries grafted into the spleen of untreated animals, after a treatment of 2 months there were in the considerably enlarged ovaries beside the developing follicles numerous corpora lutea of a larger size and a longer span of life than the normal one.

On the contrary, treatment with a daily dose of 10 μ g follicle hormone markedly inhibited the secretion of follicle stimulating hormone (FSH) since only sporadically were there mature or normally developing follicles, resp. corpora lutea beside a few atresic follicles in the uncommonly small ovary grafts in the spleen.

Daily administration of a dose of 500 to 800 μ g testosterone inhibited not only the secretion of FSH but also that of the luteinizing hormone, because 64 per cent of the ovary grafts in the spleen necrosed and were absorbed without leaving a trace, or were transformed into connective tissue. In the 9 grafts in which development had set in, normally developing follicles occurred only occasionally and corpus luteum not in a single case.

Acute manifestation of latent Addison's disease after operation in a case of heterotopic adrenal gland

Margit Dávid, G. Kardos

(Dept. of Pathological Anatomy and 1st Dept. of Surgery, Medical University, Szeged)

Operation for inpatid disease of the liver was followed by intractable hypotension, gradually developing anuria, and death. On necropsy, the left adrenal gland was found to be paper thin (adrenocortical contraction), the right one was missing, while in the right lobe of the liver acutely necrosed microscopical nodules consisting of adrenal cortical tissue were revealed. In the adenohypophysis, the basophil cells are decreased in number while there was a moderate increase in the number of the eosinophil cells.

This case has several noteworthy features.

1. The conditions found in the adenohypophysis, the lymphatic organs, and the adrenal glands, suggest that a latent insufficiency of the adrenal cortex had been present for a long time without clinical symptoms. The operation representing a trauma resulted in the acute necrosis of the single functioning adrenal gland whereby the latent failure of the heterotopic organ became manifest.

2. This case is unparallelled with regard to the presence of adrenal tissue in the liver combined with the complete absence of the adrenal gland on the same side. Thus, the adrenal gland found in the liver was not an accessory one but a true heterotopic adrenal of exceptional rarity.

Effect of the adrenals on liver regeneration

Éva Horváth, K. Kovács

(Dept. of Pathological Anatomy, Medical University, Szeged)

In 120 white rats of the same strain, of both sexes, kept on the same diet, the effect of the adrenal gland and cortisone on hepatic regeneration and on the capacity of the serum of hepatectomized animals to enhance mitotic activity, were examined. In the experimental animals, partial hepatectomy, bilateral adrenalectomy, cortisone administration, intraperitoneal administration of the serum of hepatectomized animals, and combinations of these procedures were carried out.

The cytologic examination of the liver was performed 24 and 30 hours after hepatectomy, 48, 96, 102 and 108 hours after bilateral adrenalectomy, 30 hours after cortisone injection, and 24, 30, and 36 hours after the administration of hepatectomized serum. Of each liver the cells of 200 visual fields were counted at a magnification 1 : 900, then the mitotic index was calculated from the values obtained (number of mitoses : 10 000). The following results were obtained.

1. Partial hepatectomy gives rise to intensive regeneration.

2. In normal animals, cortisone administration results in the cessation of mitosis, in hepatectomized animals it reduces the intensive mitotic activity.

3. The enhancing of mitotic activity by intraperitoneal administration of animals hepatectomized serum was completely prevented by cortisone.

4. If the serum of animals subjected to hepatectomy and treatment with cortisone is given to normal rats, the liver of the latter will be devoid of mitoses.

5. Following bilateral adrenalectomy the mitotic index in the liver is considerably higher than normal. This effect is most marked 48 hours, and ceases about 100 hours, after adrenectomy.

These examinations have pointed to a retardating action of adrenals and cortisone on hepatic regeneration. In the opinion of the authors, this action depends on the inhibitory effect of cortisone on protein metabolism.

The examination of the luteinization effect of infantile rats in parabiosis

Gy. Illei

(Dept. of Anatomy and Histology, Medical University, Pécs)

In two infantile rats, aged 60 and 30 days respectively, have been sutured to each other, castration of the 60-day-old animal resulted in the enlargement of the ovary of the 30-day-old intact animal. This ovary, however, contained no corpus luteum but growing follicles only. Conversely, if the 30-day-old partner had been castrated, the ovary of the 60-day-old rat killed on the 10th day after suturing displayed enlargement of the ovary and numerous corpora lutea. If both rats brought into parabiosis were 30 days old, the castration of one animal resulted in intensive luteinization in the ovary of the other rat after the 13th day of parabiosis, while up to the 12th day no corpus luteum could be revealed in the intact animal.

These examinations show that, if infantile rats are living in parabiosis, the luteinization of the ovary of the intact animal depends on its own age only. The age of the castrated partner has no influence on the process.

Choline esterase activity in degenerating and regenerating motor end-plates

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The methods of estimating choline esterase activity of the end-plates i. e. the naphthyl acetate, indoxyl acetate and thiocholine methods, were compared. The behaviour of the subneural apparatuses of rats following denervation was examined with the thiocholine method. In a first series of examinations it has been shown that the choline esterase activity of the subneural end-plates persists for 180 days after denervation. In the meantime, the structure possessing enzymatic activity undergoes cytochemical changes (hypersegmentation, fragmentation, granule formation).

In a second experimental series the choline esterase activity of the regenerating motor end-plates was studied. The first signs of regeneration appear 180 days after the interruption of the nerve ; groups made up of small disks (3 to 4 μ in diameter) appear, showing an intense choline esterase activity. In a later phase the disks become fused whereby subneural apparatuses exhibiting a high choline esterase activity develop. Since the process of regeneration always takes place at the site of the end-plate fragments, or close by them, it is suggested that the enzymic activity of the degenerating end-plates may exert a directing action of the growth of regenerating fibres.

Surgical application of synthetic substances and bioplasts

M. Gerendás

(Central Research Institute of the National Blood-Transfusion Service, Budapest)

In addition to the widespread surgical use of permanent prostheses and interposits made of synthetic substances, the application of materials remaining at the site of implantation temporarily only, i. e. not longer than during the regeneration of the tissues, has come to be felt as an imperative necessity.

Experiments made in this respect have shown one of the serum proteins, namely fibrin, to be most suitable for the purpose. Implants made of fibrin, therefore of natural origin, do not behave as foreign bodies in the organism, and their shape and rigidity warrant correct regeneration. After regeneration is complete, they are first decomposed by the action of tissue enzymes, and then absorbed by the organism.

We have given the name "bioplasts" to this group of artificial substances of natural origin. The surgical application of bioplasts (as tubes, capsules, caps, nails, plugs etc.) is in progress.

Absorption of implanted "Fibroplast"

D. Bagdy, D. Áfra, M. Gerendás

(Pharmacoindustrial Research Institute, State Institute of Neurosurgery, State Blood Donor Service, Budapest)

Absorption of, and tissue reactions produced by, fibrin films made with trombin and fibrinogen of great purity isolated from cattle plasma were examined in 120 animal experiments. The film used were partly normal ones sterilized in an autoclave at 120° C, partly films pretreated with different plasticizing substances. They were implanted in dogs, cats, rabbits, and rats.

The cell reaction elicited by the implanted fibrin films varied in dependence on the absorption phase. Cells were actively partaking in the dissolution of the film. After absorption has been completed the cell reaction disappears. The time of absorption is independent of the site of implantation. Films implanted into damaged tissue or a muscle wound are absorbed at a greater speed than those placed in an intact muscle. The absorption time is proportionate to the protein content of the film and depends on its physico-chemical pre-treatment (duration of heat effect, application of chrome corrosion etc.). The cell reaction is, according to the microscopic findings, not stronger than that observed by other authors using fibrin films of human origin.

In further animal experiments, the aptitude of fibrin films for the replacement of the dura mater and the use of preformed fibrin tubes in the suturing of peripheral nerves, were studied. The authors contend that fibrin films, being indifferent to living tissues, completely absorbable at controllable rate and capable of separating regenerating areas, lend themselves to wide use in neurosurgery.

Experimental neoplasty of the common bile duct by fibrin tube

Zs. Pataky, R. Gergely, Gy. Mérei, A. Csillag, M. Gerendás

(1st Dept. of Surgery and 2nd Dept. of Pathological Anatomy, Medical University, and the State Blood Donor Service, Budapest)

The final provision of injuries to the common bile duct is one of the unsettled problems of surgery. In dogs an excised part of the choledochus, or the whole duct was replaced by a fibrin tube. Fibrin proved indifferent, both locally and to the whole organism. It did not give rise to irritation. Within 8 to 9 month the fibrin tube implanted to the place of the duct underwent complete absorption. In the meantime, it became encapsulated by a connective tissue layer, but mucous membrane proliferated from the choledochus stump toward the newly formed biliary duct only in part of the cases. This was presumably due to an inadequate technique: the mucosa of the stump had been brought in junction with the outer surface of the fibrin tube, so that it was unable to proliferate into its lumen. The common bile duct of the dog being very

narrow, it is extremely difficult to introduce the mucosa in the lumen of the fibrin tube. All the dogs in which no mucosa had developed, died, because the new tube devoid of lining was compressed by scar tissue to such an extent that bile flow was stopped. In some cases, biliary cirrhosis developed. Dogs in which the mucosal lining of the new tube had been secured, survived. The number of the experiments does not permit final conclusions, but it has been established that fibrin is a non-irritant, readily absorbable substance, the employment of which on a wide basis is recommended. The application of a fibrin tube for replacing the common bile duct is still in an experimental stage and its practical use depends on the possibilities of surgical technique, the goal being to prevent the shrinkage of the newly formed duct.

Utilization of skin graft and fibrin film to fill soft part defects in the chest wall

T. Remete, I. Kiss, O. Székely

(Army Central Hospital and Outpatient Clinic, Budapest)

In perforating injuries of the chest wall the main surgical problem is the closure of the open pneumothorax. This is difficult in case of a large defect, and the application of the usual procedures (muscle graft, diaphragmopexy etc.) frequently fails.

In dogs, thoracal defects measuring from 5 by 5 to 5 by 10 cm were prepared and it was tried to cover them partly with free autoplastic skin grafts, partly with fibrin film from cattle plasma. 23 dogs were used in the experiments with the following result. Records and histological preparations are demonstrated.

Skin graft and fibrin film adhered well to the parietal pleura and became built in.

Skin grafts have the advantage of being autoplastic living tissue, readily available, and easily sutured. On the other hand, they have the drawback of the tendency to cicatrization and shrinkage. In some cases epithelial cysts also formed, wherefore later half thickness grafts were used instead of skin grafts. The fibrin film has likewise the advantage of simple availability and tissue indifference. It is rapidly absorbed without injurious cell reactions, and soon replaced by young connective tissue. Above this coat, endothelial pleura also can form while the schrinkage is comparatively mild. The film has the drawback of fragility, wherefore its use demands much patience and a careful technique. The importance of fibrin films of greater resistance is stressed

Experiments for the applicability of polyvinylchloride in surgery

E. Hedri, Gy. Mérei, S. Drobni, L. Zolnay

(1st Dept. of Surgery and 2nd Dept. of Pathological Anatomy, Medical University, Budapest)

The artificial substance V—10 a polymer of polyvinylchloride with 10 per cent dibutylphthalate for softening, was examined in animal experiments. V—10 results initially in the promotion of periosteal callus formation. Later on, callus formation diminishes, and bone atrophy may even occur. Round the implantate, small white cell collections, foreign body giant cells, homogenization of muscle fibres were observed. In dogs, V—10 exerted no toxic effect during the first six months. However, in the animals sacrificed after 14 month, the liver contained foci of fatty and hydropic degeneration, and accumulations of haemosiderin, though no clinical signs of these changes had been apparent. There were parenchymal degeneration in the kidney and cell mobilisation and haemosiderin collections the spleen. Experiments on dogs, rats, and mice, revealed a chronic toxicity of the substance, wherefore it should not be employed in surgery. Presently, the cause of its toxicity is unknown ; this is, otherwise, a chemical problem. On the other hand, there are reports on PVC preparations which have been employed in surgery with much success. Obviously, regarding the mode of their production and their chemical properties, they must greatly differ from that used in our experiments. Since we have examined the substance V—10 only, we have no opinion on PVC in general. Our only purpose was to report on our unfavourable experience with the PVC derivative V—10.

Experimental thoracic plombage made of artificial resin chips placed in a nylon capsule

G. Bakó, Gy. Bornemisza

(Dept. of Surgical Anatomy and Operative Surgery, Medical University, Debrecen)

Chips falling off at preparation of experimental endoprostheses from polymerized methyl methacrylate were wrapped into a nylon texture (women's stocking), and the egg-sized plugs obtained were put into the chest of 20 dogs, in order to observe their relationship to the adjacent tissues. The chips of artificial resin underwent dissolution while being kept in acetone in the course of embedding. In the sections, gaps were found in their places, and, round the gaps, connective tissue bundles consisting mainly of collagen fibres. Vascularization of the plugs was examined by the intraarterial injection of indian ink and subsequent clarification in artificial Gaultheria oil. A great number of new centripetal vessels was demonstrated.

Operation for abdominal hernia with polyamide net alloplast

Gy. Dávid, R. Kós

(1st Dept. of Surgery, Medical University, Budapest)

During the last year superpolyamide nets were applied in 19 cases of large abdominal hernia to replace tissue defects or to strengthen the sutures uniting atrophic muscles or tendons. Round this net connective tissue proliferates and the scar plate produced in this way prevents the recurrence of hernia. Out of 19 cases recurrence was observed in one instance only. In another case a late silk-thread fistula occurred. The net was probably not responsible for any of these complications. In the other cases healing was undisturbed and the result is lasting.

Artificial dura grafts

D. Áfra, Gy. Fényes

(State Institute of Neurosurgery, Budapest)

Replacement of the injured or tumorous dura is often a problem. Beside homoi-plastic grafts (fascia lata, galea), artificial ones are frequently employed. Out of the numerous substances reported, polyethylene and fibrin plates seem particularly adequate for this purpose.

In the Institute, fibrin film was applied in 15, polyethylene plate in 25 cases to replace dura defects.

The advantages and disadvantages of the two substances may be summarized as follows.

1. Fibrin film becomes completely absorbed without any tissue reaction, within the time defined by the pre-treatment.
2. It prevents meningo-cerebral adhesions.
3. It is translucent, well pliable.
4. It does not give rise to postoperative local reactions. It has the disadvantage that it cannot be sutured, wherefore it cannot be used to the closure of intermeningeal spaces or to retain herniated brain parts. Polyethylene is free of this drawback of the fibrin film, as it can be sutured. However, it often gives rise to postoperative local reactions for which reoperation may be neccessary.

Thus, neither of these substances possesses all the qualities expected from an ideal dura graft, so that their use is in each case a matter of consideration. The final solution of the problem needs further investigations.

Fate of vegetable substances used in vessel grafting

H. Jellinek, I. Csillag

(2nd Dept. of Pathological Anatomy, Medical University, Budapest)

On the infrarenal section of the vena cava inferior an artificial defect measuring 10 to 15 mm in length and 6 to 8 mm in width was made. The defect was covered with the fibrous meshwork of wax-covered plant parts. The vegetable graft restored the continuity of the vessel, circulation was undisturbed after operation. Further experiments are being made to examine the organism's reaction to the vegetable graft.

Three dimensional representation of the brain's angioarchitecture in corrosion preparations made of artificial resin

G. Szikla, B. Zolnai

(State Institute of Neurosurgery and Dept. of Anatomy, Medical University, Budapest)

The corrosion procedures and substances hitherto used have failed to fill and demonstrate the intraparenchymal vessels of the brain. A new procedure was devised by use of artificial resin. In this manner it became possible to represent the finest vessels of the brain parenchyma in corrosion preparations i. e. in three dimensions. Owing to its low viscosity, the substance can be injected under low pressure. Its solidification takes place without loss. The preparation is an exact copy, without artefact, of the vascular system. The differences in the angioarchitecture of the different brain parts have been demonstrated on the preparations presented.

Results of cranioplasty with acrylate derivatives

Gy. Fényes, J. Kepes, Gy. Szabó, J. Szénásy

(State Institute of Neurosurgery, Budapest)

After infavourable results in replacing defects on the cranial vault with different substances, acryl plates have been introduced for that purpose. In two years, over 20 such operations were carried out. The results were both statically and cosmetically satisfactory and no complication whatever has occurred due to the artificial substance. On reoperation for other causes, there was opportunity to examine the environment of the artificial graft and the tissue reaction produced.

Implantation of acrylate teeth-roots

Z. Hegedüs, G. Inke

(Postgraduate School of Dentistry, Budapest)

Roots composed of either pure, spontaneously binding acrylate, or macerated spongy substance combined with acrylate (as recommended by Heiss) were implanted in dogs on the site of previously extracted teeth.

All implants consisting of pure acrylate were eliminated within 2 to 4 weeks, without signs of inflammation. Implants fixed to neighbouring teeth by means of splints remained longer in the alveolus but were eliminated as soon as the splints were removed.

On the other hand, the incidence of taking of implants composed of macerated spongy substance combined with acrylate was 50 per cent, as proved by X-ray examinations and histology. In the case of acrylate-implants the epithelium of the gingiva was found to have grown down to the bottom of the alveolus, and granulation tissue rich in cells was encountered beneath. No such epithelial growth developed with implants consisting of spongy tissue and acrylate and organisation took place by means of connective tissue poor in cells. The macerated spongy substance was not absorbed within 3 to 7 month.

The X-ray examination of a one-year old case, which has not yet been subjected to histological analysis, points to the probability of fresh spongy tissue being formed in the area of the implants.

SECTIONAL MEETING

I. Forensic medicine

Does traction exerted on the umbilical chord give rise to respiration?

K. Beöthy

(Dept. of Forensic Medicine, Medical University, Pécs)

In careful experiments it has been demonstrated that traction on the umbilical chord does not promote the access of air to the alveoli of the lung of the stillborn.

Skeletization time of foetuses after intrauterine operations and under experimental conditions

I. Gy. Fazekas

(Dept. of Forensic Medicine, Medical University, Szeged)

A 30 years old woman, on whom an intrauterine operation had been performed by a physician at the end of the 5th month of her pregnancy, died 62 hours after the intervention. Necropsy 24 hours later revealed peritonitis, a two-fingerbreadth complete tear of uneven border above the inner orifice, and in a cavity of the size of a man's fist, situated between the membranes of the right broad ligament, the skeleton of a 5-month-old foetus embedded in a purulent-fibrinous mass. The bones of the right lower extremity were seated in the cervical canal, the foot hanging through the outer orifice into the vagina. On this foot the soft parts were still present. Of the other parts of the body, only the bones were found, except for the lower limbs on which the ligaments of the joints were preserved. Of the muscles and inner organs not even the slightest traces could be detected. The individual bones were covered with some yellowish-brown greasy substance. From the uterus and the vagina a dirty-red, malodorous discharge was oozing. The question arose whether the time elapsed from the intrauterine manipulation to the necropsy had sufficed for the skeletization of the foetus, or whether this had taken place earlier. To settle the problem 20 fresh foetuses of different age were kept in a thermostat at 38° C. Complete skeletization took

24 to 43 hours at the age of 3 month (9 to 10 cm body length),
21 to 44 hours at 3,5 month (12 to 14 cm),
40 to 72 hours at 4 month (15 to 18 cm),
39 to 72 hours at 4,5 month (20 to 22 cm),
53 to 72 hours at 5 month (24 to 26 cm) of age.

In 9 of the 10 cases hitherto published skeletization of the foetuses aged 3 to 4 month took from 10 to 20 days; one foetus 5 month of age became skeletized in 22 hours. Thus the skeletization of the foetus under consideration may well have come about in the time of 86 hours elapsed between the intrauterine operation and necropsy. The rapid skeletization was undoubtedly promoted by autolytic tissue ferments, and, to a greater extent, by the fermentative activity of the puscells and the putrefying bacteria. In the experiments destruction of the soft parts was due to tissue ferments and bacterial putrefaction.

Violence to children

Mrs. L. Dános

(Dept. of Forensic Medicine, Medical University, Pécs)

Report on lethal and non-lethal cases.

The relationship between sudden death in infancy and weather changes

E. Somogyi, I. Takács

(Dept. Forensic Medicine and 1st Dept. of Paediatrics,
Medical University, Budapest)

In 156 cases of sudden death in infancy in which at necropsy little or no morbid change had been found it was examined by Schelling's method whether weather or front changes exert, aside from the chance a statistically significant influence on sudden death.

Thrown objects

K. Kerekes

(Dept. of Forensic Medicine, Medical University, Pécs)

Mode of injuries by thrown objects.

Examination of dust-covered corpora delicti

L. Dános

(Dept. of Forensic Medicine, Medical University, Pécs)

Report on the medicolegal examination of dust.

Further investigations concerning chemiluminescence

J. Nagy

(Dept. of Forensic Medicine, Medical University, Debrecen)

Relying on his previous preliminary investigations, and using an apparatus of his own design, the author determined the character of light emitted by 3-aminophthalic hydrazide with blood.

Measurements have proved that with blood the light is specific. First its intensity is great, but than it diminishes rapidly until the 120th second, after which the decrease in intensity is slow.

Simultaneously, the properties of the luminescence caused by various metals (iron, copper) was also determined and it has been concluded that they differ not only from metal to metal but from metals to blood as well.

The experimental results indicate that the chemiluminescence-test, used at present for purposes of information only, could be made specific for blood.

The role of histochemical reactions in the estimation of the time of injuries

Gy. Farkas

(Dept. of Forensic Medicine, Medical University, Pécs)

The value of histochemical reactions in estimating the time of injury has been discussed. The reactions allow to determine whether the injury had been afflicted during life or post mortem.

Paper chromatography in lethal poisoning with barbiturates and a quick method for their demonstration

Erzsébet Császár, O. Szücs

(Dept. of Pharmacology, Dept. of Forensic Medicine, Medical University, Budapest)

In cases of lethal barbiturate poisoning, barbiturates have been successfully demonstrated from fat tissue. On the basis of Raventos' examinations (1954), in the cadaver this method seems to be more adequate than the examination of blood, urine, or gastric contents. To date, partition paper chromatography has not yielded proper results.

The quick method runs as follows. Fat tissue is melted in a hot water bath ; in this way, liquid fat is obtained which is of medium viscosity even at room temperature. It is shaken with lye, slightly acidified, then extracted with chloroform under shaking. The chloroform is placed onto a filter paper previously prepared with an 1 per cent solution of cobalt nitrate. After evaporation of the chloroform the filter paper is developed by Marschall's method in ammonia gas. Sensitivity of the method is 10 μg.

Umbilical sepsis

S. Ökrös

(Dept. of Forensic Medicine, Medical University, Debrecen)

Thirtyfive cases of umbilical sepsis encountered in the material of the Institute in the course of 4 years have been worked up both histologically and microbiologically. The clinical course of the disease had been more or less identical in every case. The predominant symptoms on which the clinical diagnosis had been based had been those of meningitis, jaundice, pneumonia, and sepsis, umbilical infection having escaped attention. At the clinico-pathological discussions it has therefore been emphasized how important it was that a physician should be present when the newborn are bathed, and that he should watch the navel until the stump of the umbilical cord has become detached. No more cases of umbilical sepsis have since then been encountered at necropsy, as infections of this kind are now recognized early and adequate therapy is applied in due time.

The infants in question had been born in the 8th or 9th of the pregnancy with a weight of from 1050 to 3750 g. They lived from 2 to 30 days. In 7 cases the umbilical cord was not yet clearly demarcated, while suppurating navel wounds were encountered in the rest. The infection spread along the skin of the abdomen or the umbilical vessels through the lymphatic system, sometimes through the umbilical veins. A combination of these paths of infection was also encountered.

As a rule, Ps pyocyanea was isolated from the area of the inflamed navel (Dr. *Melles*, Dr. *Herpay*), though diplococci, too, were found in the smears.

The 35 cases examined ought to serve as a warning for the practician that the demarcation of the umbilical cord should carefully be watched, and that, at the appearance of even the slightest alarming symptom, the danger of umbilical sepsis should be borne in mind.

Artery arrosion attending the penetration of a caseous lymph node into a bronchus

L. Tamáska, R. Budvári

(Dept. of Forensic Medicine, Medical University, Budapest)

A rather infrequent complication of the bronchial penetration of caseous lymph nodes in old patients is reported. The authors observed repeatedly at the necropsy of old individuals who had died suddenly that the bronchial penetration of caseous lymph nodes was accompanied by an aneurysm-like protrusion of a branch of the pulmonary artery into the bronchus. The rupture of the protruding part resulted in blood aspiration and suffocation.

Mycologic examination of the lung of infants died suddenly of bronchiolitis and pneumonia

A. Dósa

(Dept. of Forensic Medicine, Medical University, Szeged)

30 infants who had died a suddenly death between 1953 and 1955 were examined post mortem. Death had mostly been due to bronchiolitis and subsequent focal pneumonia, less frequently to interstitial pneumonia. Pieces of the lungs removed under sterile conditions were explanted onto Sabouraud's rigid malt agar and blood agar slants. Only fungi grew on the media in 19 (63 per cent) cases, fungi and bacteria in 5 (10 per cent), only bacteria in 4 (10 per cent), no microorganism in 5 (10 per cent) cases. The majority were Blastomycely. The fact that fungi grew in a much greater number than bacteria is remarkable. Their incidence is probably even still greater considering that there were cases in which fungi failed to grow on the culture medium although were found in the histologic sections. It is believed that fungi play a prominent part in the genesis of infants' pneumonia. They may have a primary role, in other cases they aggravate pneumonia of bacterial origin. Lethal bronchiolitis is, in the author's view, due to the allergic response of the lung to the action of fungi ; this may causes death if its development is rapid. In cases with a negative culture the viral origin must be taken into account. Investigations should be carried out in this direction.

Haemoptysis of central origin

L. Tamáska, L. Harsányi

(Dept. of Forensic Medicine, Medical University, Budapest)

In cerebral circulation disorders, e. g. arterial thrombosis on the brain basis, survival after hanging, and nontraumatic alterations of the skull, patchy haemorrhages in the lung parenchyma were observed associated with interstitial emphysema and air accumulation in the right half of the heart. From the periodic respiration and interstitial emphysema during life it was concluded that cerebral dyspnea was present and, consequently the pulmonary haemorrhages of central origin were produced apart from neurovascular factors, also by respiratory-mechanical ones. Due to the latter may pulmogenic air embolism arise. Since these lung haemorrhages constitute favourable conditions for the formation of inflammatory foci, a revision of the so-called haemorrhagic pneumonia is thought necessary.

Contributions to the pathogenesis of subendocardial haemorrhages

L. Harsányi, A. Árvay

(Dept. of Forensic Medicine, Medical University, Budapest)

500 cases of subendocardial haemorrhage were observed in the authors necropsy material. On the basis of statistical evaluations, the haemorrhages in cases of natural death were not separated from those associated with violent death. Instead of this, two groups were formed according to whether the subendocardial haemorrhage was an isolated phenomenon or a partial one attending purpura. By dividing the material in this sense it was found that in 281 cases isolated subendocardial haemorrhage occurred with a lesion of the central nervous system (trauma, apoplexy, embolism etc.), whereas in 219 cases general purpura (due to burning, poisoning, liver damage, fat embolism etc.) was also present. From a pathogenetical point of view, isolated subendocardial haemorrhages only should be investigated.

Spontaneous tear of the papillary muscle

A. Árvay, L. Takácsy

(Dept. of Forensic Medicine, Medical University, Budapest)

The break of a musculus papillaris is a rare complication of myocardial infarcts, whereby a nacute valvular failure arises and the condition deteriorates. In 6 cases the cause and mechanism of the tear were examined. In the authors opinion, the occurrence of the tear depends on the location, depth, and extension of the infarct. Histotopographic examinations will be carried out in order to clear these factors.

Experimental contributions to the spontaneous tear of human papillary muscle

A. Árvay, L. Takácsy

(Dept. of Forensic Medicine, Medical University, Budapest)

In the first series of the examinations, one of the papillary muscles of the right ventricle of dogs was cut and the changes following this operation were examined in order to obtain data to the evaluation of the changes found in human cases. The broken part freely moving in the ventricle may probably give rise to some modification of the basic histologic phenomena. Further, it has been tried to state the time order of the changes. Similar examinations are being performed with the papillary muscles of the left ventricle.

Death during operation and pituitary tuberculosis

L. Tamáska, L. Takácsy

(Dept. of Forensic Medicine, Medical University, Budapest)

In the initial stage of an operation for myoma carried out with adequate technique, sudden death occurred. At necropsy, ancient caseous foci were found in the lungs. Microscopic examination revealed tuberculous granulation tissue in the hypophysis and epiphysis. The thyroid was diminished in size and so were the adrenals. The sudden death during operation might have been due to the disorders of blood pressure regulation resulting from the changes of the endocrine organs. Among the causes of death, hypofunction of the endocrine glands may often play a role, as shown also by the present case.

SECTIONAL MEETING

II. Morphological Subjects

Changes in the innervation of the adrenal marrow

Gy. Botár

(State Institute of Neurology and Psychiatry, Budapest)

The microscopic structure of the innervation of the adrenal marrow in young healthy dogs, very old dogs, and young dogs kept at a vitamin deficiency diet, was compared on the basis of silver impregnation preparations. Aging is accompanied by reduced innervation and alteration of the remaining nerve fibres. Avitaminosis results in diminished innervation and severe changes of the nerve fibres. Other influences (fever, starvation) are followed by varying changes of the innervation. The changes occurring with age and other influences show that not only the afferent but also the efferent innervation are influenced by the organism and the environment.

Nerve supply of teeth and their environment

D. Hattyasy

(Dept. of Stomatology, Medical University, Szeged)

In the pulpa, periodontium, and the gingiva of calves, swine, and rats, impregnation procedures display the presence of nerve fibres of at least two different thickness. Mostly, they run together. The fibres passing to the odontoblasts appear in the pulpa at a relatively late period of development. Prior to this, only single fibres are seen near the vessels (rat) or in the form of perivascular plexuses (swine). The continuously growing incisor of the rat behaves like a developing tooth, thus its innervation is scanty and primitive.

In the periodontium (mainly in rats) two kinds of nerve endings are found, viz. simple endings (probably pain receptors) and end apparatuses (probably for localization).

The gingival epithelium is supplied by thin and medium-sized fibres which are partly single, partly forming a mesh.

The subepithelial connective tissue of the gingiva is abundantly innervated. The majority of the fibres pass to the surface through the marrow cavities.

New sensory end apparatuses in the sclera of mammals

A. Ábrahám

(Institute of General Zoology and Biology, University, Szeged)

By the application of Bielschowsky—Ábrahám's silver impregnation, in the sclera of cattle (Bos taurus), sheep (Ovis aries), goat (Capra ibex), deer (Cervus elaphus), roe (Cervus capreolus), horse (Equus caballus), and hare (Oryctolagus cuniculus), sensory plexuses of varying

shape, abundant tree-like branchings, and, on the latter, peculiar neurofibrillary end plates of great extension were found. These sensory elements are, in all of the examined animals, seated in the inner coat of the sclera, the lamina fusca. Although both forms of ending may be found in each individual sclera, the greatest amount of them are present in the sclera of cattle and it is here that they can be best demonstrated.

Generally, the plexuses are elongated, loosely woven, their main fibres are thick, with bulgy varices. As a rule, they develop from the end system of the fibres but there are also plexuses on the bundles. The tree-like ramifications which mainly in cattle occur in masses at the place mentioned, are formed partly from the end branch system of single fibres, partly by the interweaving of the end branch systems of several thick fibres, but invariably in a manner that the end fibres preserve their independence. The latter terminate in round, oval or irregular neurofibrillary end plates best visible in the sclera of cattle. Some of the end plates are remarkably large and the neurofibrils are distinctly observable in them. The neurofibrils are relatively thick in both the fibres and the end plates, their location and interrelations are varying and characteristic of the individual forms. The end organs are probably receptors for pain or the pressure of the aqueous humour.

Contributions to the histotopography of the ganglion sublinguale

I. Nagy, H. Woronkoff

(Dept. of Anatomy, Histology and Embryology, Medical University, Szeged)

The variable appearance and topography of the sublingual ganglion was examined in man.

In the trunk of the sublingual nerve, near its origin is situated a ganglion of an average length of 9 mm. Beside this, 3 to 9 small ganglia measuring from 0,1 to 0,9 mm in length have been found in or around the branches passing to the sublingual gland of the nerve. (Photomicrogrammes and a reconstructed figure are presented.)

The total size of the small ganglia has been compared with that of the submandibular ganglion of well-known location, by counting the ganglion cells.

Submicroscopic structure of the connective tissue fibre systems and the interstitial substance, and their relation to the pathology of vessels

Gy. Romhányi

(Dept. of Pathological Anatomy, Medical University, Pécs)

On the basis of the anisotropic staining of connective tissue fibres and acid mucopolysaccharides, characteristic polarization optical differences are displayed by the various types of connective tissue fibre. The acid mucopolysaccharides, which are considered a homogeneous interstitial substance, display a fibrillary structure of high orientation (aorta, cornea, granulation tissue). The polarization optical method employed, combined with enzymatic examinations (hyaluronidase, elastase), yields new possibilities for the recognition and characterization of the submicroscopical structural changes of the mucoid substance in normal and sclerotic vessels.

Contraction and syneresis of collagen fibres

Ilona Banga

(1st Dept. of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

Native collagen fibres can contract when exposed to the action of heat or certain chemical substances. This contraction is like the physiological contraction of muscle fibres i. e. the thickening of the fibres is proportional to their reduction in length. If, however, the bond of procollagen and metacollagen combining in the collagen fibre is destroyed or if the procollagen is extracted

from the fibre, heat or chemical action will result in syneresis instead of contraction. Syneresis manifests itself in the uniform shrinking of the fibre in all dimensions, while water is expressed from it. Thus, physiological contraction and the syneresis of proteins devoid of structure are opposite phenomena.

Aging of collagen fibres

D. Szabó and Ilona Banga

(1st Dept. of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

It has been shown in earlier experiments that at room temperature (18° to 20° C) in a 40 per cent potassium iodide solution collagen fibres are capable of contraction and relaxation. With this method called chemical contraction-relaxation the collagen fibres of rats of different age were examined.

A significant change of the chemical contraction-relaxation was found proportionate to the age of the animals.

Basal membrane made up of glycoproteid round the peripheral nerve

P. Röhlich

(Dept. of Histology and Embryology, Medical University, Budapest)

It has been shown in earlier examinations that the diffusion barrier around peripheral nerves is a cellular membrane which was termed prilemma. This membrane composed of several layers was examined with histochemical methods (periodic acid-Schiff-reaction, alone and after lipid extraction, treatment with hyaluronidase and diastase, further metachromasia, methylene blue extinction). The perilemma has been found to consist of a vasal membrane containing glycoproteid, and flat cells covering the membrane on both sides.

Polarization optical examination of collagenous fibre systems in tuberculous structures

J. Kurucz, J. Szőke

(State Tuberculosis Institute, Budapest)

The changes of collagenous fibres occurring in caseous foci and cavity walls can be studied by the polarization optical method.

The phenol-concentrational birefringency curve of necrotizing fibres becomes protracted, due to the reduced capacity of the fibres to absorb phenol. The assumption that a normal fibrillar structure may be associated with a decreased phenol absorbing capacity, has been proved in a model experiment.

The reduction of the phenol absorption capacity of the collagenous fibres in tuberculous structures or in the model experiment is real, against the apparent reduction of this capacity of the fibrinoid. In the case of the latter the protraction of the curve is due to the additive optical effect of fibrin-collagen.

Changes of elastic fibres in pulmonary tuberculosis

E. Vincze

(State Tuberculosis Institute, Budapest)

In caseous foci part of the elastic fibres retains its normal structure; their majority, however, exhibits signs of decay and degeneration. On the basis of the elastic fibre structure, the tissue involved by caseation can mostly be recognized. The elastic fibres stain with fuchselin, safranelin or orcein. Haematoxylin stain often results in a light blue colour. At the border of caseation, close by the specific granulation tissue, fragments of circular elastic fibres are often found. These structures do not always correspond to a preformed tissue, wherefore it may be assumed that the fragments of fibres undergo a re-arrangement in caseous-necrotic areas.

Experimental changes in argyrophil fibres

F. Bölönyi, Piroska Balla

(Dept. of Anatomy, Medical University, Debrecen)

The experimental changes of argyrophil fibres were examined in frog tongues. 202 tongues were worked up.

Physical and chemical effects were applied: burning, freezing, histamine, congestion, acid, lye, formalin, electric shock, X-ray irradiation, turpentine.

The changes observed may by divided in three groups.

a) Local numerical increase and thickening of fibres resulted from the application of burning, histamine, and artificial congestion. Thickening was particularly considerable after histamine or congestion. The increase and thickening of fibres due to congestion occurred mainly around the vessels.

b) Diffuse extensive changes occurred after acid or lye treatment. The changes were of different degree *(Smirnova—Zankova)*. In some cases the fibres were broken up and thickened. Later, apparently after a stronger action of the agent, fusion and homogeneization ensued. In diffuse changes the periodic acid-Schiff reaction was negative, unlike the result observed with the local increase of fibres.

c) Local increase and thickening of fibres with extensive homogeneization. This double change occurred after electric shock, formalin administration, and, to a lesser extent, X-ray irradiation.

Further contributions to the structural stability of nucleinic acids

K. Jobst

(Dept. of Pathological Anatomy, Medical University, Pécs)

At the last session of this Society the observation was reported that in a weak acid medium (pH 3,8) tissue nucleinic acids lose their original negative birefringency, due to the decomposition of the transverse lamellar structure. It was found that nucleinic acids show special anisotropic properties on staining with certain dyes. This made it possible to study under the polarization microscope in histologic sections the acid resistance or depolymerization of nucleinic acid chains. The effect of n-HCl acting for different length of time on the polarization optical behaviour, in dependence on the intactness of the chain, and its cessation, were examined. Quantitative comparisons were also made on the basis of the intensity of Feulgen's reaction. The curve of Feulgen's reaction was followed with a certain retardation by the cessation of anisotropism. Comparative examinations of the stability of nucleinic acids following acid treatment were performed on pyknotic nuclei, and nuclei of tumour cells. Significant differences were observed in these examinations.

Histochemical demonstration of urease, ammonia and urea

F. Freisinger, I. Jakab

(1st Dept. of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

Up to date, urease was demonstrated in tissues by Sen's technique. The effect of urease results in the decomposition of urea to ammonia and carbonate. Sen's method consists in that a tissue sample is incubated in a solution of the substrate (urea), then the produced carbonate is precipitated with cobalt nitrate. *Glick*, criticizing this method had proposed to make the enzyme act not on the whole tissue piece but on a section only, as with the phosphatase reaction. This task has been accomplished by the authors. Their method of embedding does not inactivate the enzyme. The section is incubated in a mixture of urea and cobalt nitrate. The specificity of the method was shown by the sections incubated without the substrate, in cobalt nitrate only. At the same time, a histochemical method for demonstrating the other decomposition product, the ammonia, has also been devised. The pure ammonia released at the areas where urease is present is traced by two tests, termed direct and indirect Nessler-test, respectively. The localisation of urease established by this method is the same as that recognized by the demonstration of carbonate (Sen's method modificated by *Freisinger*). Finally authors devised a modification of Löffler's test for the histochemical demonstration of urea.

A new method of knife-freezing (with demonstration)

G. Inke

(Dept. of Anatomy, Medical University, Budapest)

A new type of knife-freezing appliance is presented in which the carbon dioxide is introduced into a cavity formed within the knife. Cooling is thus prolonged to 4 to 7 minutes (according to external temperature), with a carbon dioxide-fedding of 15 seconds.

The fate of spermia not partaking in fertilization

Z. Pósalaky, Gy. Hajdi

(Dept. of Histology and Embryology, Medical University, Budapest)

It has been reported at the last Congress on the fate of rat spermia introduced in the uterus. It was found that they invaded, in a large number and within a short time, the uterine wall. In this lecture, the fate of spermia ejaculated into the female under natural conditions was examined. The spermia stained with carbol-fuchsin preserved their colour even after intensive treatment with acids. This property allows their demonstration in tissues. They preserved the colour after they had lost their shape. By means of this method they can be observed in tissues for a longer time than it was possible before.

The load on the hip joint resulting from transverse "grand écart"

M. Nemessuri

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On extreme straddling ("grand écart") the trunk comes in contact with the soil. The limbs are, partly under the effect of body weight, in forward and backward extension, respectively, in the sagittal plane. The hip joint of the leg in front is in flexion-abduction-outward-rotation. In this position, the majority of the ligaments and muscles surrounding the joint are greatly extended.

Starting from the data of *Ivanitsky* and *Sarovatov*, the effect of extreme straddling on the hip joint and its holding and moving apparatus was examined in 5 male and 5 female students of the School. Motions and tension of the acting muscles were recorded with photography and X-rays. The data have shown that girls are more likely to learn this exercise, due to their looser muscle and ligament apparatus. Once the exercise has been learned, it is performed by boys and girls without a demonstrable difference.

If the exercise is carried out after proper preparations, the elasticity of some muscles around the hip joint increases. At the same time, the joint capsule is extended without the danger of hyperextension. Thereby, the conditions of the hip joint become more favourable for other sports (football, hurdle race etc.) and also for motions occurring in everyday life.

Spirometric examinations in cadaver lungs

E. Berki

(Dept. of Pathological Anatomy, Medical University, Pécs)

The respiratory capacity of the lungs was examined with spirometry, with special regard to emphysema and induration. Spirometric curves of adult healthy lungs were compared with the curves of emphysematous lungs. Hereby, the reduction of elasticity resulting in partial or total expiratory failure became conspicuous. The curves allow some conclusion as to the degree of the emphysema, and the quantitative characterization of its initial patterns. From the curves of indurated lungs the inspiratory resistance can well be read.

Histophysiology of the anterior hypothalamus—neurohypophysis system in traumatic oliguria

D. Bachrach, S. Scultéty, J. Jáki, B. Korpássy

(Dept. of Pathological Anatomy and 1st Dept. of Surgery, Medical University, Szeged)

The antidiuretic centres were studied with histophysiological methods in rats in tourniquet shock.

In the first series, the development of oliguria was followed by a biological method. Following the application of tourniquet, the animals, hydrated at the same time, excreted for 3,5 hours a lesser, though gradually increasing, quantity of urine than the controls. After this time antidiuresis appeared and persisted after the removal of the tourniquet, then ceased in 24 to 48 hours.

In the second series, the histologic pattern of the antidiuretic centres was examined in the various phases of tourniquet oliguria. The histophysiological picture was estimated by a method devised in earlier experiments. Soon after oliguria had set in, tissue changes pointing to hyperfunction occurred in the antidiuretic centres. The histological signs of hyperfunction persisted for several days in both the anterior hypothalamic nuclei and the neurohypophysis.

The two phenomena are, in our view, interrelated : beside the deterioration of circulation the intense neurohormonal (vasopressor-antidiuretic) reaction demonstrated in tourniquet shock has a role in the development of oliguria.

Changes in the cytologic architecture of the nephron after hypophysectomy and adrenalectomy

I. Kádas

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In previous examinations the functional and morphologic changes in the cat kidney occurring on exsiccosis and adrenectomy and the functional architecture of the nephron following hypophysectomy and adrenectomy were studied. Normal animals, starving ones and animals treated with ACTH served as controls. After the 2nd day of hypophysectomy the fat content

increased in both the proximal and the distal section of the nephron. This quantitative change was unaccompanied by structural changes in the proximal section. In the ascending part of Henle's loop, progressive decomposition of the submicroscopic lipid-protein structure appeared on the 3rd day, manifesting itself microscopically as a fine-granulated fatty transformation. By means of a special anisotropic stain the decomposition of the intracellular lipid-protein meshwork could be observed in detail. According to these observations, while the intracellular protein framework is preserved, desorientation of the lipid component resp. its detachment from the protein framework is the essential feature of the process.

These changes were rather pronounced on the 4th to 5th postoperative day. After adrenectomy, similar changes were observed on the same section of the nephron. These were, however, slight on the 4th to 5th postoperative day, i. e. there was no parallelism between the changes mentioned and those following hypophysectomy.

Luteinization effect and pituitary histology

Vera Bárdos, B. Flerkó

(Dept. of Anatomy, Histology and Embryology, Medical University, Pécs)

Castrated rats were brought in parabiosis with intact ones. In the ovaries of some of the latter luteinization was induced. The quantitative histologic analysis of the hypophysis of both partners has shown, that in agreement with earlier literary data, castration of the rat results in a considerable increase in gonadotrophic activity, with a slight reduction of the number of acidophil and chromophobe cells, a simultaneous increase in the number of basophil and periodic acid-Schiff positive cells, and the formation of castration cells.

On comparing the hypophysis of luteinized and non-luteinized intact partners, there was no systemic correlation between the obviously increased LH production of the luteinized animals and the percentage of basophil, periodic acid-Schiff positive, or acidophil cells.

Quantitative determination of thyreotrophic hormone in organs from experimental animals and cadavers

B. Mess

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Jacobj's nucleus variation statistical method allows a far more accurate estimation of thyreotrophic hormone in the thyreoid gland one-day-old chicken than does the hitherto used determination of thyroid weight. By the method, the difference in thyreotrophic hormone contained by the half pituitary of an untreated rat, and one pretreated with daily 5 μg of thyroxin for 2 weeks, is readily demonstrated.

By the method thyreotrophic hormone was determined in pituitary glands taken from human embryos of different age. In this way, the development in time of the thyreotrophic function of the human pituitary can be observed and compared with the development of the cytologic architecture of the organ.

Innervation of blood- and lymph capillaries

F. Kiss

(Dept. of Anatomy, Medical University, Budapest)

By a prolonged silver impregnation a rich meshwork of nerves can be demonstrated on the blood and lymph capillaries. The lumina of both kinds of capillaries are not uniform, there being wide and narrow sections alternately. In this respect, capillaries resemble the large pulmonary veins on which alternate contractions and dilations. By this a rosary-like

picture is produced. The narrow sections of the blood capillaries are functional phenomena accounting for the so-called aggregate formation, that is, capillaries may, under nervous effects, contract to such a degree that only the serum can pass while the erythrocytes form aggregates at the wider sections.

Comparative histological examinations of the architecture of the wall of lymph capillaries

M. Poberai, A. Gellért, I. Nagy, S. Nagy, J. Lippai

(Dept. of Anatomy, Histology, and Embryology, Medical University, Szeged)

The thoracic duct, great lymph trunks and peripheral lymph vessels were examined in man, goat, cattle, swine, dog, cat. and rabbit. H-E. Crossmon's (acid fuchsinanilin blue), van Giesen's and resorcin-fuchsin stains were employed. The results obtained in several thousand sections were as follows.

The thoracic duct and the great trunks display, in regard of the structure of the wall, three different types, in man and animals alike.

(i) *type :* smooth muscle and collagen fibres predominate (man, goat).

(ii) *type :* smooth muscle and elastic fibres prevail (calf, swine).

(iii) *type :* there are only a few or no muscle elements (dog, cat, rabbit).

The three coats (intima, media, adventitia) are pronounced in types (i) and (ii) only.

Intima : it consists in all types of endothelium and little connective tissue. In type *ii* there is a marked elastica interna.

Media : in type (i) and (ii) the muscle coat is made up of 2 or 3 layers (circular and longitudinal). In type *ii* they are separated by elastic fibres. In type (iii) muscle elements occur in the lower section of the thoracic duct only.

Adventitia : Well distinguishable in type (i) and (ii). In type (i) it is mainly composed of collagen fibres, in type (ii) there are in addition intermingling elastic fibres. In type (iii) the adventitia composed of collagen fibres and a few elastic membranes merges with the surrounding connective tissue.

As to the *peripheral lymph vessels*, two types can be distinguished, in agreement with *Baum* and *Kihara* (1929):

1. such as contain more or less muscle fibres (i) and (ii) duct group), and
2. those containing only a few, or no, muscle fibres (iii) duct group).

Photomicrogramms of all types are presented.

The innervation of lymph vessels

A. Gellért, S. Nagy, J. Lippai, M. Poberai

(Dept. of Anatomy, Histology, and Embryology, Medical University, Szeged)

The innervation of the thoracic duct, lumbar trunks, mesenteric and other peripheral lymph vessels, was examined after supravital methylene blue staining and silver impregnation.

1. The nerves of lymph vessels derive, as a rule, from vessel-nerve bundles and attain the lymph vessels partly along with the vasa vasorum, partly independently of the latter.
2. Nerves form on lymph vessels loose plexuses.
3. In the plexuses more amyelinic and less myelinic fibres are found.
4. The amyelinic fibres end with very fine terminal plexuses. The picture is identical with that of the terminal basic plexus depicted by *Hillarp* and considered by time the characteristic form of innervation in smooth muscle.

The function of arterio-venous anastomoses

Gy. Tarján, F. Kiss

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A model experiment was designed to imitate the action of arterio-venous anastomoses. In the course of the model experiment the following observations were made.

1. Constriction above the origin of a branche secures a suction effect. Fluid circulation in the model is continuous.

2. Artificial constriction on the precapillary section results in "recirculation" i. e. opening of the tube system representing an arterio-venous anastomosis, whereby a shunt is developed.

Microscopic examination of the lymph vessels of muscles

M. Kozma, A. Gellért

(Dept. of Anatomy, Histology, and Embryology, Medical University, Szeged)

The lymph vessels of muscles were examined by the injection technique, and by artificial congestion in the lymph vessels of various animals.

In the injected preparations, true lymph vessels were very rarely seen in the perimysium, probably because of the forced injection and the damaging effect of the dye.

The congested lymph vessels were generally found in the neighbourhood of blood vessels. Their calibre was small in the internal perimysium and larger in the external perimysium. Between the individual muscle fibres or bundles no lymph vessels with an own wall were seen.

These results support the opinion according to which lymph circulates first freely between the muscle fibres. In contrast to the uncertainty about this point, the above examinations have proved that lymph vessels possessing an own wall are formed in the internal perimysium.

Procedure for the roentgen-anatomic and roentgen-pathologic study of thoracic structures

Mrs. Mária T. Rácz, J. Kurucz

(State Tuberculosis Institute, Budapest)

The vessels of excised lungs were filled with consolidating radioopaque substance, then, after fixation, sections 1 to 2 cm thick were placed in lead nitrate solution. The X-ray picture taken from these sections displays in the form of opacities of different degree the morbid changes simultaneously with the vessels and bronchi, and the interrelationship of these structures. The procedure suits itself well for filling the vessels and bronchi and the mediastinal lymph nodes with radioopaque substance, allowing a study of the roentgen anatomy of the mediastinal lymph node system making it possible to obtain roentgen-anatomic pictures with intense contrasts.

SECTIONAL MEETING

III. Pathology

Generalized moniliasis associated with acute leucosis

Márta Mosonyi

(County Hospital, Győr)

In recent literature, increasing attention is paid to local and generalized fungal diseases which since advent of antibiotics have become more and more frequent. The two are apparently somehow correlated, although there were a few cases in which this correlation could be excluded with certainty.

The case reported is that of a 52-year old woman who had repeatedly been in hospital for non-characteristic symptoms. Differential blood counts and sternal bone marrow showed an acute leucosis. Because of a pyogenic process on the skin and mucous membranes, penicillin therapy was instituted. Since the process was not influenced and exudative-necrotic changes also occurred in the mouth and pharynx, administration of penicillin was continued for a long time, until the death of the patient.

Necropsy revealed a thick, pseudomembrane-like coating in the areas mentioned, and in the entire length of the oesophagus, with a few nudes necrotic foci. On the jejunal mucosa there were about pea-sized superficial nodules covered by a dark-brown crust or with a necrosed surface, while on the skin of the sacral, gluteal and perianal regions numerous millet-sized infiltrated pustules were seen. It was particularly the oesophageal process which was suspicious of mycosis, aside from the fact that in both lungs widely scattered infiltrated foci could be palpated, the appearance of which did not correspond to inflammation.

Histology proved the presence of mycosis. The fungus proved to be Candida albicans. It was found not only on the surface but also in the deeper layers. Though there were no means to identify the microorganism by cultivation the changes observed left no doubt as to its pathogenic role. It has been concluded that the pathogenicity and spread of the fungus were related to the 18 million units of penicillin administered.

In the reported case, the generalized moniliasis subsequent to penicillin treatment in the course of the acute leucosis had little influence on the fate of the patient. However, the possibility of moniliasis as a complication of antibotic therapy must not be disregarded, all the more since antimycotic drugs administered together with the antibiotics can often prevent such lethal complications.

Fungus infestation of extreme degree with antibiotic therapy

Erzsébet Hársfalvy, Gy. Szutrély, Gy. Dévai

(2nd Dept. of Pathological Anatomy and 1st Dept. of Paediatrics, Medical University, Budapest)

In a 5-year old girl, panmyelopthisis of unknown origin dated back to one year. On admission, 3 weeks before death, typhoid fever displaying septic symptoms was established. Aureomycin was administered and hibernation instituted. Necropsy revealed an extensive fungus coat in the alimentary tract. In the bone marrow the number of reticulum cells was increased and there

was no haemopoïesis. In the lymph organs, especially the lymph follicles of the small intestine, extensive reactive reticulosis was present. Stress has been laid on the correlation of aureomycin therapy and the grave infestation with fungi, which proved Blastomyces. The rôle of hibernation in the development of mycosis has been discussed.

Histologic diagnosis of blastomycosis

J. Baló, Gy. Róna, Judit Temes

(1st Dept. of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

The problem of aetiology often arises when chronic inflammation is found in histologic specimens. Among the biopsy material examined at the Institute, in 17 cases a yeast-like fungus was found in the sections. In 3 other cases similar fungi were found at examination of necropsy material. The diseased organs yielding fungi were the skin, bones, joints, middle-ear, bronchi, lungs, endocardium, lymph nodes, ovary, anus. The occurrence of such fungi in granulation tissue is a sign of their aetiologic rôle. This rôle can be proved through cultivation or inoculation into white mice. Cultivation was successful in three cases in which the agent was Cryptococcus neoformans, Cryptococcus Gilchristi, and Cryptococcus Laurentii, respectively. It is contended that the antibiotic control of bacterial infections may result in an increased incidence of mycosis.

Granulation produced by different fungi

J. Molnár

(State Railways Hospital, Budapest)

The development of granulation tissue induced by Cryptococcus neoformans, Blastomyces dermatitidis, and Candida albicans, was examined in man and experimental animals. It has been found that the granulation tissue cannot be regarded as characteristic of the individual fungus strains. However, a certain arrangement within the granulation foci may be considered typical of the individual strains. The demonstration of the agent is important with respect to histological diagnosis. To this end, the periodic acid-leucofuchsin stain is appropriate if it is employed correctly and with due criticism. The structure of the granulation tissue depends on the chemical composition of the capsule of the agent. Pertinent examinations are being carried out.

Investigations into the pathomechanism of hepatitis

I. Sümegi, L. Goreczky, I. Róth

(State Railways Hospital, Budapest)

In the history of patients died of fulminant hepatitis earlier diseases involving liver damage were mentioned in 85 per cent. The role of these diseases was proved by model experiments, in a way that rabbits treated with various liver poisons were allowed to heal and then poisoned again. For the pretreated animals 1/12 of the lethal dose was fatal, whilst the control survived. It is assumed, that in the cytoplasm of the damaged liver cells pathologic proteins develop, which subsequently are absorbed and act as autoantigens, giving rise to sensitization of the organism. This sensitization would, after repeated damages, result in a rapid destruction of the liver tissue. The demonstration of this autoaggression was performed by an indirect approach. Organ shock was induced in the liver by poisoning the rabbits with phosphorus, chloroform, and hepatotoxic serum. After nephelogramms and biopsy had shown restitution, the extract of a similarly poisoned liver was injected into the portal circulation. This injection was followed

as a result of shock effect by the reduction of bile excretion to 48 per cent. In the control animals, the injection resulted in a 6% decrease of bile excretion. In the histologic specimens shoal liver cell damage resembling fibrinoid necrosis was seen. In the experiments it has been ascertained, that the antigens meet the auto-antibodies. It is therefore believed, that the coloured proteins, which appear in the liver cells after trichrome-staining, arise from the antigen-antibody reaction. In man, the above demonstrated allergic reaction may have grave sequels.

Morbid anatomy of epidemic hepatitis

I. Besznyák

(1st Dept. of Pathological Anatomy and Experimental Cancer Research, Medical University, Budapest)

The morbid changes occurring in epidemic hepatitis were examined from 1951 until 1955 both in the necropsy and the biopsy material of the Institute. Necropsy was done in 44 cases of epidemic hepatitis, of which 13 had run a fulminant, 17 a subacute, and 14 a chronic course.

Biopsy material was examined in 29 cases of epidemic hepatitis and in 10 cases of homologous serum hepatitis. In these cases inclusion bodies were sought for.

The relations of epidemic hepatitis to catarrhal jaundice, yellow atrophy of the liver, and liver cirrhosis have been discussed on the basis of own observations and literary data. Further, aetiologic problems, the correlations of epidemic and homologous serum hepatitis, finally the problem of inclusion bodies have been dealt with, together with the problems of prognosis and restitution.

Histologic changes in the liver and brain of dogs with infectious hepatitis

P. Kapp

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Several cases of infectious hepatitis in dogs has been observed by the author in recent years. He succeeded in transmiting disease from dog to dog through 15 passages. It has been shown by cross immunization experiments that the disease is not identical with dog's distemper, a fact pointed out by *Green*, *Rubarth*, *Parry* and *Larin*, *Hudson* and *Mansi*, on the basis of their experiments on polecats.

The majority of the experimental dogs died on the 3rd to 7th day after inoculation. The main changes were enlargement of spleen and liver, oedematous imbibition of the wall of the gall bladder, haemorrhages in the stomach and the intestines. Under the microscope serous or serous-haemorrhagic inflammation foci were seen, occasionally with centrilobular necrosis, in the liver. Further, intranuclear inclusions were found in the parenchyme cells and the endothelial cells of the intrahepatic vessels, in the same form as reported by *Rubarth*. Mild cerebral changes consisting in ring-chaped perivascular haemorrhages and mononuclear infiltrations, further regressive alterations of varying degree in the nerve cells, were revealed in 4 of the 10 brains examined, whereas these changes were rather severe in 1 brain. Similar changes were observed in the brain of three young foxes infected with the virus of canine hepatitis, which died on the 2nd or 3rd day after the infection. The brain process found in the dogs and foxes were much the same as those observed by *Levaditi*, *Schoop*, *Sompolinszky* etc., in the so-called fox-encephalitis described by *Green*. Thus, the results of the author agree with those of the inoculation experiments of *Siedentopf—Carlson*, further *Svenkerud*, by which the identity of the two diseases has been demonstrated.

The epidemic hepatitis discussed differs from human infectious hepatitis. The microscopic changes of an acute character in the liver point to a rapid course. The intranuclear inclusions nearly invariably found in liver and endothelial cells have not been mentioned by the researches of human hepatitis, except by *Nicolau*.

Listeria encephalitis in sheep

Gy. Sályi, G. Hirt

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The bacterium termed Listeria monocytogenes revealed from laboratory rodents by *Murray*, *Webb*, and *Schwann*, produces two forms of disease in domestic animals. In rodents, poultry, and embryos of various animals, it gives rise to a kind of septicaemia accompanied, if the course is not rapid, by inflammatory necrotic foci in the liver and other organs. In swine and ruminants, it causes most frequently encephalitis.

Listeria encephalitis of the sheep was first reported by *Gill* (1931—1933) from Australia who established its identity with the so-called circling disease. Since then, the process has been recognized in different parts of the world and also in this country (*Mócsy* and *Sályi*, 1952). No cases were noted between 1952 and 1955. Early in 1955, it was observed in over 25 stocks. This fact shows that the disease is not infrequent in Hungary.

The inflammatory changes of the brain were found to be roughly identical with those reported by *Gill*, *Jungherr*, *Pallaske*, *Biester* and *Schwarte*, *Fish* and *Schroder*, etc. They are most marked in the brain stem (pons, oblongata, corpora quadrigemina) and the cerebellum. The perivascular mononuclear infiltration containing a few granulocytes resembles that found in viral diseases. More characteristic are the focal infiltrations of ectodermal tissue in which polymorphonuclear leucocytes predominate. In the foci, rodshaped bacteria resembling the agents of swine erysipelas are found after Gram or Giemsa staining. Within the foci, the nerve fibres are destroyed, the cells display a grat variety of degenerative processes. The site of the changes and the bacteriologic examinations made post mortem admit the conclusion that the agents gain access to the brain by the blood current.

In human pathology few cases attributable to Listeria infection were reported. Recently, their number has been increasing. The infection may manifest itself with encephalitis (*Burn*, *Webb* and *Barber*, *Seeliger*, *Ödegaard* and al., *Seeliger* and *Leineweber*, *Simon* etc.), or, in the newborn and young infants with the formation of inflammatory-necrotic foci in the organs (*Reiss*, *Potel* and *Krebs*, *Seeliger*, *Seeliger* and al., *Gagemann* and al., *Schmitz* etc.). Listeria infection bears some relation to the infectious mononucleosis of man.

Lipoidoses of the nervous system

(Neurohistologic changes in gargoylism)

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In a 5-year old child with oligophrenia characteristic signs of gargoylism (Hurler'disease) were present (typical face and skull, hepato-splenomegaly etc.). All nerve cells of the brain exhibited the same typical change : swelling of the cell body and, frequently, of the dendrites (especially the apical one), local spindle-shaped or round swellings on the dendrites. The alteration of the dendrites was most pronounced in the Purkinje cells of the cerebellum, and the upper layers of the cerebrum. The swollen nerve cells stained with Scarlet R were filled with a yellowish-red granular substance, the tone of which was not the same in every nerve cell. The glia cells, especially those of the microglia and oligodendroglia, were filled with a similar lipid substance. In the adventitia of the vessels only a few cells contained these scarlet-positive granules, and their colour was bright red. The elements of the vessel wall and the leptomeninges contained no lipid, they stained with haematoxylin a pale bluish-grey and a pale grey with Bielschowsky's silver impregnation. The best demonstration of the lipids resulted from Perdrau's procedure, a sign that the matter contained in the cells was made up of lipids and proteins. The relation of the changes to those found in Tay-Sachs' disease is discussed.

Cystic changes in the brain

L. Nagy, M. Fehér

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The brains from 6300 necropsies performed in the above department and the County Hospital at Székesfehérvár were examined with special regard to cyst formation. Cysts and pseudocysts were found in 200 brains. Beside the more frequent cysts due to bleeding, softening, decay of tumour, trauma etc. rare formations e. g. porencephaly (5), ependyma cyst of the 3rd ventricle (1), cysts in the lateral ventricles (2), brain cyst due to developmental anomaly of the skull, were also observed.

The literature on the classification of cystic and pseudocystic changes *(Virchow, Bruns, Fraenkel* and *Lemke)* is reviewed and criticized, and it is suggested to consider an aetiologic grouping with respect to topography.

Multiple degenerative (avascular) emollition in the brain

Katalin Haberland

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A case is presented in which the clinical diagnosis had been : state after laparotomy done for intraperitoneal abscess, toxic encephalopathy, questionable encephalitis. On gross examination, there was no change in the nervous system. In the histologic sections of the gray and white matter innumerable emollition foci were found, without perivascular infiltration, vessel wall alteration or lumen obturation. This is a rare cerebral complication of a local infection.

Inclusion bodies in ganglions in leukaemia

L. Molnár, E. Kerekes

(2nd Dept. of Pathological Anatomy, Medical University, Budapest)

The changes occurring in the nervous system in leukaemia were investigated with regard to the pathogenesis. First, the spinal ganglions were examined, because :

1. They are of great significance for the trophic innervation of the organism,
2. the pertinent literature is scanty,
3. they display the most severe and conspicuous changes. To date, the ganglia taken from 3 cases of lymphoid leukaemia and 2 cases of myeloid leukaemia were examined.

The most noteworthy changes were the inclusion bodies found in groups in the cytoplasm of the cells of cervical, dorsal, and lumbar ganglia, in 4 of the examined 5 cases. In 2 acute cases they were particularly numerous. Special stains allowed to differentiate the inclusions from all other morbid structures. In all of the cases, other regressive phenomena, too, were observed which resulted in the destruction of the majority of ganglion cells. In two cases in which the clinical diagnosis of leukaemia has not been corroborated by necropsy (leukaemoid reaction), no inclusions were present.

Nerve element changes in congenital megacolon

Gy. Gorácz, J. Szekér

(2nd Dept. of Pathological Anatomy, Medical University, Budapest)

The examination of 5 cases has shown that distally from the dilated section in the part of the colon which on gross examination is apparently of normal width, no ganglion cells are present. In the place of the submucous and intramuscular nerve elements, thick bundles of nerve fibres are found. At the junction of the two sections atypical ganglion cells may be seen.

In the course of long-standing disease the normal ganglion cells of the dilated section also undergo degenerative changes due to inflammation and mechanical irritation, whereby Swensson's operation, if performed in late childhood, may fail to bring about restoration.

Myoblastoma granulocellulare vulvae

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(Bajcsy-Zsilinszky Hospital, Budapest)

In the presented case, Abrikosoff's tumour appeared at an unusual place, in the skin of the labia majora. Histotopographical and histochemical features of the tumour are discussed, together with its histogenesis, with special regard to the resemblance of this tumour and mesenchymal storage diseases. Finally, the differential diagnosis against xanthoma and onkocytoma is discussed.

Inactivity atrophy in vessels

A. Temesvári, L. Fodor

(Postgraduate School of Surgery, Medical University, Budapest, and State Institute of Rheumatology and Balneology, Budapest)

Functional changes lead to structural changes. Hypofunction and hyperfunction result in atrophy or hypertrophy, respectively. Changes of the systolic pressure or the pressure amplitude in arteries (e. g. in coarctation of the aorta, stenosis of the pulmonary artery) are presumably followed by atrophic or hypertrophic changes in the arterial wall. From this point of view have experiments been carried out and has the clinical material been studied. The proximal and distal section of the arteries were examined in cases of coarctation of the aorta, pulmonary stenosis and arterio-venous shunt. Above the stenosis, increase in the number and thickening of the elastic fibres were found. At the section of diminished pressure, the number of elastic fibres was reduced, they were thinner and stained unevenly. In parts of the vessel wall at areas with increased pressure accumulation of metachromatic mucoid substance was found. Atrophy occurred not only immediately below the stenosed part, but also far from it, at places where no whirl effect could have a rôle. It is thought that post-stenotic dilatation is due mainly to the drop of pressure and that the rôle of whirls is secondary. The clinical observations have been confirmed through experiments.

Effect of nuclear poisons on the resting cells of organs

Late L. Matkó, L. Holczinger, S. Keresztúry

(State Institute of Oncology, Budapest)

The effect of colchicin, podophyllin, and nitrogen mustard, was examined on the nuclei of liver, kidney, and myocardium cells.

Beside histological examinations, the variance of nuclear size was recorded by measuring and by nucleus variation curves.

Karyometry has shown that all the three substances exert a significant influence on the size of nuclei. The changes manifest themselves in the diameter, volume, and surface, alike.

The changes in nuclear size are rapid and reversible.

All of the three substances are capable to produce so-called cell inclusion bodies in the liver, still more in the kidney. These "inclusions" are regarded as pathologic transformations of nucleoli. No such structures occurred in the cells of the heart muscle.

On the basis of these examinations it is contended that the so-called karyoclastic substances act, beside the dividing ones, also on the resting cells. The action manifests itself, beyond the prohibition of mitosis, with changes in the nuclear size. These substances are therefore considered general poisons of nuclear metabolism.

Changes in joint tissues during pregnancy

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and Municipal Hospital, Budapest, Uzsoki utca)

In rheumatology it is a well-known fact that pregnancy influences the course of the diseases of motion organs. One of the present authors treated patients with Bechterew's disease with gonadotropin (Lutocrescin). In non-advanced cases there was pronounced improvement.

To clarify some problems of this effect, rat experiments were carried out. The spinal column was examined histologically in 20 pregnant and 20 non-pregnant rats. The McManus-Hotchkiss reaction demonstrated the storage of acid mucopolysaccharides in the intervertebral disks.

Fibrinoid changes in the ganglions of joints

M. Németh-Csóka

(Dept. of Pathological Anatomy, Medical University, Pécs)

The problem of fibrinoid changes occurring in the wall of articulation ganglions (para-articular mucinous cysts) is unsettled. It was found that hyaluronic acid isolated from synovial fluid and chondroitin sulfuric acid from septum nasi of ox by precipitation exhibit the same staining properties including anisotropic staining with accridine compounds as the inner part of the wall and fibrinoid areas in the articulation ganglions. It seems therefore, that these areas contain mucopolysaccharides in increased amounts.

Hand—Schüller—Christian's disease

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The disease is rare in the adults. In the case of a 31 year old woman, diabetes insipidus was the only sign of the classical syndrome which had presented itself during life. At death the clinical diagnosis was miliary tuberculosis and toxic exanthem. At necropsy the flat and shaft bones displayed the classical pattern. There was a light, yellow, ointmentlike mass in the pea-sized and larger bone defects of the skull, in the vertebrae and the bones of the limbs. Throughout the body, the lymph nodes were enlarged, they contained numerous foci of granulation tissue, some of which contained lipids. In the lungs the foci stimulating miliary tuberculosis consisted of perivascular and interstitial granulation tissue containing no lipids. In the yellow foci of the bones destroying the osseous substance lipid storing foamy cells and cholesterol crystals were present which stained rust-brown with Sudan III, proved birefringent and Schultz-positive.

In the opinion of the authors, development of lipid-free granulation occurs in the early stage of the disease. Later, lipids appear in the cells. After the cholesterol containing histiocytes had necrosed the lipids are found extracellularly, often in the form of characteristic crystals.

On the basis of the histologic pattern, granulation in the disease, is considered the primary in the disease whereas the disorder of cholesterol metabolism is held secondary.

Contributions to the pathology of fat tissue

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In a 19-year old girl with hypertension due to phaeochromocytoma, the removal of three hazelnut-sized tumours had been followed by a rapid drop of blood pressure and death. At necropsy, peculiar changes were found in the fat tissue of the parietal pericardium, renal capsule, and round the abdominal aorta. The fat was mahogany-brown and displayed glandular-lobular structure. The subcutaneous fat was yellow, the bone marrow fat was normal, both in character and location. Histology revealed beside the usual signet-ring shape fat cells two other types. One of them was large, swollen, with numerous equal vacuoles in the cytoplasm. In the vacuoles, birefringent lipids were found. The other type was polygonal or bearing processes, the cytoplasm was in the unstained specimens brown, contained fine argentaffin and chromaffin granules. A similar case was reported by *Feyrter*, who also observed brown fat tissue in similar distribution in a 19-year old man who had died of phaeochromocytoma. The present authors hold the tissue to be specially differentiated fat, whereas Feyrter called it common brown fat tissue. Histologically, this fat has a certain resemblance to the adrenal marrow or the paraganglia. The peculiar change may have been due, like in Feyrter's case, to the pressor substances produced by the phaeochromocytoma. The chromaffin granules found in the cells indicate the deposition of a special substance which may be adrenalin or noradrenalin, since the tissue extract exerted a pressor effect.

Significance of the fatty transformation of the pancreas

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On the basis of the histologic examination of 250 human pancreases, attention is called to the problem of lipomatosis of the organ. The process involves the excretory system and there is consequential pseudohypertrophy of the islands. In 47 per cent of the cases lipomatosis was considerable and in 15 per cent it was extensive and it had destroyed the majority of acini. With respect to aetiology, histogenesis and prognosty the cases of lipomatosis should be devided in three groups, viz

1. Fatty degeneration,
2. Fat deposition,
3. Fatty metamorphosis.

The three forms are discussed in detail. The greatest importance is attributed to the third form which represent, unlike the cases of fatty infiltration or degeneration, a special local destruction of the parenchyma by autodigestion. The histologic phases of this metamorphosis can be traced by staining procedures. Necrosis of the acini, microcyst formation and the development of fat cells, are the main phases, as already described by other authors.

The possibility of post mortem changes has been excluded. The fact that senile atrophy is more extensive in the pancreas than in other organs, is ascribed to the effect of digesting juices acting along with injuries involving the whole organism. It has been found, that the resistance of the gland is impaired mainly by local arteriosclerosis, less frequently by the trophical disorder due to congestion. It is for this reason that lipomatosis so a frequent and severe diabetics is. The clinical significance of the process is discussed.

Osteogenesis imperfecta

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Two cases are reported.

Case 1 was a premature boy of 1270 g weight and 38 cm length. Case 2 was a girl aged 3 weeks ; she was 42 cm long and weighed 3500 g. On gross inspection, the deformities and fractures characteristic of osteogenesis imperfecta were seen on the limbs.

X-ray examination also revealed typical signs such as thin cortex, reduced calcification, numerous ancient and recent fractures, callus formation. In the area of the calluses the calcium content of the bones was increased. The ossification foci had not been affected by the process.

Histology. In the bones of the cranial vault, the tabula externa and interna had not developed, in their place fibrous tissue was found. The cortex was very thin, not uniform, no cancellous bone was present, the marrow was scanty. Round the fracture of the rib and in the area of the callus, there were relatively well ossified bone lamellae in an irregular arrangement, which did not unite to cancellous bone. Below the periosteum a cartilaginous callus was present with deficient ossification and fibrous marrow. The essential feature of the disease could be studied on the sections of the vertebrae. The architecture of the cartilage and the development of the directing cartilage rows were normal. Ossification was deficient, due to the deficient or sluggish production of basic substance by the osteoblasts. The number of the osteoblasts was apparently normal, but the lamellae were surrounded by a thin ossified border only. A peculiar change was observed in the muscles : between and around the muscle bundles immature tissue of mesenchymal origin was found. The muscle substance displayed a focal or diffuse lymphocytic infiltration, whereby the very thin muscle fibres had been detached from each other or discontinued.

Authors contend that in the disease in question all mesenchymal tissues may be involved. This has been confirmed by the alteration of the muscles ; an analogous case was observed by Rössle.

Developmental anomalies of the gallbladder and the bile ducts

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11 cases were revealed in 3800 necropsies. In 4 cases other developmental anomalies were also present. The longest life of 7 month was attained by 2 infants. In these cases the mode of fat digestion could not be established. A proved by both the clinical and pathologic observations in 5 cases, the extrahepatic anomalies of the bile ducts had led to biliary cirrhosis.

Multiple anomalies of development

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A statistical analysis of the necropsy material of the institute revealed 6 cases of multiple developmental anomalies.

1. Septal defect, atresia of the oesophagus and the duodenum, renal aplasia, adrenal hyperplasia, atresia of the vagina, polydactylia, deformities of vertebrae and ribs.
2. Anomaly of heart development, microphthalmia, cleft palate, atresia of the external acoustic meatus, polydactylia.
3. Cor triloculare biatriale with double gallbladder.
4. Female pseudohermaphroditism with adrenal hyperplasia.
5. Female pseudohermaphroditism with persisting Botall's duct, anomaly of the development of the kidneys and adrenals, anomalous course of umbilical vessels.
6. Absence of anus and rectum, rudimentary kidneys and urinary bladder.

A brief review of the aetiologic factors is given.

Cytomegalia infantum

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In order to study infantile cytomegaly, the salivary glands, kidneys, lungs, liver, adrenal glands, pancreas, and thyroid gland of infants died before the age of one year were worked up for histology.

Cytomegaly was found in 22 of 100 infants, most frequently between the age of 2 and 6 month, most rarely in premature children. It was invariably associated with interstitial pneumonia. The majority of inclusion bodies were revealed in the parotis, the submandibular glands, kidneys, and lungs. In two cases, embryopathy due to cytomegaly was suspected. The changes are characteristic on the basis of their resemblance to those brought about by the salivary gland virus of guinea-pigs, further of fluorescence examinations, the viral origin of the disease seems probable. The disease may promote the development of other infections, its generalization can, however, cause death also by itself.

Histologic changes in animals treated with triturated organs, and parasites of rodents collected from areas afflicted with haemorrhagic nephroso-nephritis

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Out of 27 specimens of Apodemus flavicollis found in Epidemy Area I, 18 displayed such renal alterations which deserve attention from the point of view of human nephroso-nephritis. In 9 of these mice cerebral changes (regressive processes in the ganglion cells, neuronophagia, oedema etc.) were also detected. Mus spicilegus living in epidemy Area II exhibited serious renal damage in 1, mild changes in 2 cases. Mice were inoculated with the triturate of Leptus larvae, Myonissus, Echinolelaps, and Ixodes. Only the 11 mice treated with Leptus larvae developed changes, but in 3 of them no morbid process was present. Severe cerebral damage (meningoencephalitis, perivascular haemorrhage) was found in 6, renal alteration like those of Apodemus associated with cerebral process in 4 animals, and renal damage alone in 1 animal.

Renal changes in adrenal failure

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The kidneys of patients who had died with the clinical symptoms of severe adrenal lesion (tbc, tumor metastasis, necrosis, haemorrhage etc.) or adrenal insufficiency, were examined.

In the majority of histologic specimens, acute nephrosis (shock kidney) was seen. This was thought to have been induced by the Addison crisis.

In three cases, acute nephritis was present and this condition had led to death through renal failure. The prominent histologic changes were found in the glomeruli, such as thrombonecrosis of the afferent arteries and the tufts, destruction of the basal membrane (high degree of dyshoria) with subsequent tubular damage. The picture is like the hyperergic alteration (of the periarteritis nodosa type) of the arterioles and glomeruli, and certain types of malignant nephrosclerosis. The latter changes may have been due to the failing protective effect of cortisone.

In three other cases chronic Addison's disease was associated with marked productive changes in the glomeruli. The latter became rich in cells, the basal membrane thickened, the mesangium exhibited extensive albuminous imbibition. These changes may be interpreted in two ways ; either the repeated Addison crises give rise to productive processes, or the chronic DOCA administration accounted for the condition. The second assumption is favoured by the fact that according to literary data chronic administration of DOCA brings about similar changes in the glomeruli of experimental animals.

Vascular and glomerular changes in leukemia

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Microscopic examination of the organs of individuals died of leukemia revealed fibrinoid necrosis of the arterioles capillaries, and the glomeruli in 12 of 40 cases (30%), fibrinous imbibition of the interstitium in 5 cases. These changes may be present in acute or chronic, myeloid or lymphoid leukaemia likewise. They occur, however, more frequently with chronic myeloid leukaemia. Age has no role in these processes, since in the vessels and glomeruli of a child aged 2 1/2 years they were quite as severe than in adults.

Vascular changes were observed chiefly in the arterioles and capillaries of the spleen, adrenal glands, kidneys, and pancreas. In the kidneys, the fibrinous imbibition of the intertubular substance and the glomerular changes were particularly studied, beside the fibrinoid necrosis of the arterioles. Initially; the tufts become swollen, a serous fluid rich in protein accumulates in Bowman's capsule, then the tufts become partially or totally homogenized, and stain like fibrinoid necrosis. Later, hyalinic transformation takes place.

Similar processes of the vessels and glomeruli were described in numerous other diseases, first of all in diabetes, but to our best knowledge, they have not yet been observed in leukemia. There are many literary data on paraproteins formed in the blood of patients with leukemia. Their presence is indicated also by the tubular lesions observed by us i. e. the structures resembling the protein casts occurring with multiple myeloma. The changes of vessels and interstitium being due to protein imbibition, the assumption is warranted that paraproteins may have a role n their genesis.

Congenital glomerulosclerosis

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On the basis of the histologic examination of the kidneys of 200 newborn and infants it has been concluded that congenital glomerulosclerosis is by no means rare as it was found in 50 of 100 newborn and in 55 of 100 infants. The process has no clinical symptoms, it is unrelated to diseases of infancy, and provided it that can be regarded as pathological it belongs to the group of developmental anomalies. The presence is related most probably to the reorganization of the kidney. In numerous papers it has been claimed that the process is morbid, and due to infections (L. Schwarz) or related to sudden death in infancy (Barrett), or a sequel of the mother's german measles in the first third of pregnancy. In the authors' opinion, these theories are unfounded.

It has been found further that cysts in the newborn kidney may originate from glomeruli. An interesting change, frequently revealed on gross examination already is the fine granular surface of the kidney. This is a sequel of postnatal development. Postnatal development may account also for congenital glomerulosclerosis. Finally, it is suggested that the term "congenital glomerulosclerosis" be discarded because of the possibility of misinterpretation, and that the expression "hyaline glomeruli in the newborn" be used.

Morphologic observations in chronic nephritis

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The organs of three individuals died of chronic nephritis were grossly and microscopically examined. In the spleen and the lymph nodes a great number of round or polyhedral cells exceeding in size the lymphoid type were revealed. In their cytoplasm acidophil globules resembling Russel's bodies were seen. According to the literature and the present examinations, these cells be related to disorders of protein metabolism occurring with chronic nephritis. The occurrences

of a disturbance of protein metabolism had to be assumed also on the basis of the extracellular protein globules present in the adrenal interstitium, the protein imbibition of cerebral vessels, and the corpora amylacea found within the vessels of the brain. These phenomena, especially the changes seen in the spleen and the lymph nodes, have been interpreted as the morphologic manifestations of an increased antibody production enhanced by the autosensibilization mechanism acting in connection with the decomposition of kidney substance.

Renal tubular lesions induced by urethane

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In 13 of 27 rabbits treated with urethane large degeneration vacuoles were found in the tubular epithelium.

Similar changes were repeatedly reported in various diseases. Of late, *Róna*, *Jellinek* and *Hollósy* reported them as necropsy findings.

The development of these changes and their assumed pathogenesis has been discussed Finally, the correlation of the spontaneous and the experimental processes has been pointed out.

The pancreas and the salivary glands in experimental anaphylaxis of guinea-pigs

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Riva and *Probst* reported in 1950 that bronchial asthma is accompanied by the inspissation of mucus in the pancreatic ducts. Starting from this report, *Farkas* examined in 1954 the pancreas and the salivary glands of 18 individuals died from asthma, and found dilated excretory ducts, hypersecretoric and dyskrinia phenomena like those on the bronchial mucosa, and fibrosis round the ducts.

To complete these observations, guinea-pig experiments were carried out. In the animals died in shock after a longer dyspnoic phase, characteristic mucinous hypersecretion was revealed in the pancreas. The goblet cells of the ducts were greatly distended, at many places confluent, and protruding toward the lumen, exhibiting in this manner the mechanism of obstruction. At the same time, other ducts were already engorged with, and dilated by, sticky mucus. Similar changes were present in the salivary glands.

These morphologic observations are in harmony with the clinical and experimental data of *Steinmann* and *Widmer* who found an increased serum diastase level in human asthma and in the anaphylactic shock of guinea-pigs, further with the results of diastase determinations performed in man by *Hajós*.

The problem of oncocyte formation

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The frequency of oncocytic degeneration and its relationships with age, sex, and various diseases, were studied by microscopic examination of 500 thyroids, 500 mammary glands, 200 salivary glands, 50 parathyroids, and 100 each of kidneys, testicles, ovaries, lungs, pancreases, intestines, larynges, paranasal cavities, pituitaries, livers, and adrenal glands. It has been found that the oncocyte is a well-defined morphological entity, readily distinguishable from every normal or morbid cell even by means of the H-E stain. The oxyphil cells of the parathyroid, the so-called Hürthle cells of the thyroid, the pale apocrine cells of cystic mastopathia, should all be regarded as oncocytes. As to the genesis of oncocytoma, this may, though much less frequently, be caused by the same effets as the oncocytes itself. No correlation was found between

basic disease and the occurrence of oncocytes. Still, strikingly, they appear almost only in organs, mainly of the neck, which are situated near each other and embryologically related, e. g. parathyroid, salivary glands, thyroid, mammary gland, upper air passages. In other organs they are rare. Another statistical fact is that oncocyte transformation is infrequent in the young. In the female it occurs particularly about the climacterium, whilst in the male mostly later, at the time of prostatic disorders. In the opinion of the authors, oncocytic degeneration is a well-defined pathological entity in which the main rôle is undoubtedly played by neurohormonal factors.

Mitochondrium conditions in the neurulation of young chicken embryos under the influence of intracellular hypoxia

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402 malformed chicken embryos were examined. Malformations were produced by the administration of 100 γ/kg Janus-green B. In 335 (83,3%) embryos developmental anomalies were found in the primitive neural and eye organ. The high percentage of conjugated developmental anomalies is a sign that, in the early period of the development of chicken embryo, there exist well-defined evolution phases responding with a particular sensitivity to the conversion of Janus green B in leukobasis. The minority of conjugated developmental anomalies occurs before the 30th hour, the majority before the 55th hour of development. Like in the observations of *Rübsaamen*, in the cases exhibiting anomalies of cerebral development the chorda dorsalis could not be traced higher than the rhombencephalic region. This may account for the fact that developmental anomalies are confined to the very area of prosencephalon and mesencephalon, further that rhachischisis is frequently found in the rhombencephalic region, often associated with schizosoma ventrale. In the embryos treated with Janus-green B, the cells of the chorda dorsalis seem between the 18th and 55th hour empty and show but a scanty mitochondrium structure, as compared with the abundant mitochondria in the untreated embryos (*Moog*, 1943). At the same time, hemopoietic islets are found in an excessive number and extension into the parenchymatous organs, with a considerable numerical increase of mitochondria.

These experiments show that in the early period of development the decomposition of Janus-green B to the leukobasis is followed by the reduction of mitochondria in the chorda dorsalis and this is followed by severe anomalies of differentiation.

Sexual prematurity of epiphyseal origin

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In the course of serial investigations, the author has repeatedly emphasized the antagonism of the epiphysis and the adenohypophysis, as also the endocrine phenomenon that this antagonism was anatomically demonstrable in humans and animals alike. In connection with the case of a sexually premature patient with a tumour of the adrenal cortex the mechanism of sexual precocity could be demonstrated anatomically. Investigating various cases of sexual precocity of endocrine origin that revealed an increased hormonal activity, the author was led to the interesting conclusion that, whichever endocrine gland was responsible for the appearance of the clinical picture by producing a pathological surplus of hormones, the disease was invariably brought about by way of the adenohypophysis, inasmuch as the equilibrium between epiphysis and adenohypophysis had been upset in favour of the latter gland. This phenomenon is well demonstrable morphologically and manifests itself also with an increase in the weight of the adenohypophysis. In a patient 21 years of age a particular endocrine factor caused premature senescence. The equilibrium between epiphysis and adenohypophysis had been upset by a cyst which, occupying the entire epiphysis, completely eliminated the otherwise unimpaired pineal parenchyma. The lesions encountered in a recent case were most remarkable in this respect. In a 13-year old boy, 174 cm tall, sexually fully mature, looking much older than his age, a cyst occupied the place of the entire parenchyma of the epiphysis and gave thus rise to sexual precocity and premature senescence.

Contributions to the pathology of generalized lupus erythematodes

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A woman 42 years of age had suffered, 18 years before her death, from febrile arthritis following tonsilectomy. 2 years before death, cardiac pain due to hypertension, then pericarditis and pleuritis had occurred. In May 1954, lupus erythematodes eruptions appeared on her face, and she developed endocarditis and nephritis. The improvement of the skin alteration was followed by chorea, then a psychosis of the exogenous type characterized by a paranoid-hallucinatory state. In the sternal punctate, L-E cells were found. There were marked dysproteinaemia and hypercholesterolaemia. The endogenous creatinine clearance became gradually less, the non-protein nitrogen level increased, and extensive oedema ensued. Death was due to uraemia.

Necropsy revealed all characteristic features of generalized lupus erythematodes, with Libman—Sacks' syndrome.

There was granular atrophy of the brain, brought about by disseminated acute and chronic necroses due to thrombosis, exudative, and proliferative changes of the small arteries and arterioles, whereby complete and incomplete necrotic foci resulted in the brain substance.

In connection with the case, the problems of the so-called collagen-vascular diseases and allergic vasculitis have been discussed.

Scleroderma with visceral changes

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The increasing frequency of the so-called collagen diseases observed throughout the world, and the recognition of efficient therapy, justify the detailed clinico-pathological analysis of these and akin patterns. In the case presented, a woman aged 56 had suffered from characteristic skin alterations and respiratory complaints. There had been nervous symptoms, and X-rays had shown a condition resembling miliary tuberculosis in the lungs. The clinical diagnosis had been generalized scleroderma pulmonary fibrosis, grave cardiomyopathy due to scleroderma and microembolisms in the brain. Necropsy and histology revealed focal fibrosis of the heart muscle, and diffuse pulmonary fibrosis. The skin corresponded to the final stage of scleroderma. There were severe changes also in the oesophagus. Severe and peculiar vessel alterations were found especially in the brain; these resulted in symmetrical necrotic areas in the nucleus caudatus.

A condition imitating Wegener's granulomatosis

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The condition found at the necropsy of a patient who had been treated for chronic nephritis and uraemia suggested the possibility of Wegener's granulomatosis. Histology did not ascertain this presumption. In a hilar lymph node typical caseous tubercles and foci with liquified centre were revealed. Similar foci were present in the liver and spleen. In addition, in some small vessels of the spleen there was an inflammation turning at places into necrosis. The majority of the renal glomeruli were cicatrized. Round most of them, and in the surroundings of some arterioles, a halo of inflammated granulative tissue had developed which consisted mainly of radially arranged epitheloid cells and mononuclear elements. In the marginal zone of the tubercles of the hilar lymph node acidfast bacilli were demonstrated. The findings were interpreted as an acute hyperergic vasculitis-nephritis on tuberculo-toxic basis, associated with the final stage of chronic glomerulo-nephritis.

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